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(54) Title: COMBINATION DRUG THERAPIES COMPRISING AMINOGLYCOSIDE ANTIBIOTICS AND N,N'-DISUBSTITUTED GUANIDINES

(57) Abstract

Methods and compositions are provided for treatment of infections, including Gram-negative and Gram-positive bacterial infections, comprising administering an aminoglycoside antibiotic in combination with a substituted guanidine or other compound as disclosed herein. Preferred methods and compositions of the invention will be effective against infections previously treated with aminoglycoside antibiotics, but with decreased occurrence of ototoxicity.

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COMBINATION DRUG THERAPIES COMPRISING AMINOGLYCOSIDE ANTIBIOTICS AND N,N'-DISUBSTITUTED GUANIDINES

BACKGROUND OF THE INVENTION

This application is a continuation-in-part of copending U.S. application serial number 60/051,860, filed July 7, 1997, which is incorporated herein by reference.

1. Field of the Invention

The present invention relates to pharmaceutical therapies that comprise administration of an aminoglycoside antibiotic in combination with a substituted guanidine or other compound as specified herein, particularly for treatment of infections such as those caused by Gram-negative bacteria.

2. Background

Aminoglycoside antibiotics have been widely used in the treatment of both Gram-positive and Gram-negative bacteria as well as against tuberculosis strains. The aminoglycosides are particularly effective against serious infections involving Gram-negative bacilli such as pyelonephritis, endocarditis, pneumonia, drug-resistant tuberculosis and sepsis. A wide variety of aminoglycosides have been previously reported. See, U.S. Patents Nos. 5,508,269; 4,645,760; and 4,380,625; and E.J. Begg et al., *Br. J. Clin. Pharmacol.*, 39:597-603 (1995).

However, aminoglycosides pose substantial toxicity problems with to about a third of patients receiving aminoglycoside therapy experience some level of hearing loss. See R.E. Brummett et al., *Arch. Otolaryngol Head Neck Surg.*, 116:406-410 (1990); S.P. Stringer et al., *Otolaryngology* (eds. M.M. Paparella et al., 1653-1669 (Saunders, Philadelphia, 1991).

It thus would be desirable to have therapies that include use of aminoglycoside antibiotics but that avoid or minimize risks of ototoxicity.

SUMMARY OF THE INVENTION

The present invention includes methods for treatment of infections, including Gram-negative and Gram-positive bacterial infections, comprising administering a combination of 1) an aminoglycoside antibiotic, and 2) with

a substituted guanidine or other compound as disclosed herein (that second component sometimes referred to herein as "compound or componds 2)").

Preferred methods and compositions of the invention will be effective against infections previously treated with aminoglycoside antibiotics, but with the significant advantage of decreased occurrence of ototoxicity relative to use of an aminoglycoside antibiotic alone.

Compounds 2) useful for administration with an aminoglycoside antibiotic in accordance with the methods of the invention have been disclosed in U.S. Patent No. 4,906,779 (Weber et al.; issued March 6, 1990); U.S. Patent No. 5,011,834 (Weber et al.; issued April 30, 1991); U.S. Patent No. 5,093,525 (Weber et al.; issued March 3, 1992); U.S. Patent No. 5,190,976 (Weber et al.; issued March 2, 1990); U.S. Patent No. 5,262,568 (Weber et al.; issued November 16, 1993); U.S. Patent No. 5,403,861 (Goldin et al.; issued April 4, 1995); and International Applications PCT/US91/03594 (Keana et al.; International Publication No. WO 91/18868); PCT/US92/0105 (Goldin et al.; International Publication No. WO 92/14697); PCT/US92/03554 (Weber et al.; International Publication No. WO 92/19621); PCT/US94/06008 (Durant et al.; International Publication No. WO 94/27591); PCT/US94/13245 (Durant et al.; International Publication No. WO 95/14461); PCT/US94/13541 (Magar et al.; International Publication No. WO 95/14467); PCT/US95/01536 (Goldin et al.; International Publication No. 95/20950); U.S. Patent application serial number 08/601,992 and International application no. PCT/US97/02678 and corresponding U.S. application serial number 08/858,399; and International Publication No. WO 98/06401. Each of those documents and the substituted guanidines and other therapeutic compounds disclosed therein are fully herein by reference. Thus, for example, preferred compounds for use in present methods include substituted guanidines include N,N'-disubstituted guanidines, N,N,N'-trisubstituted guanidines, N,N,N',N'-tetrasubstituted guanidines, hydrazinedicarboximidamide compounds, aminoguanidines, N,N-disubstituted guanidines, indolinyl and indolinyl derivative compounds, imine-substituted piperidine compound and others as disclosed below.

A wide variety of aminoglycoside antibiotics are suitable for use in the formulations of the invention. Typically, suitable aminoglycoside antibiotics contain two or more amino sugars (aminoglycosides) connected to an amino-cyclitol nucleus. Exemplary aminoglycoside antibiotics preferred for use in formulations of the present invention include clinical agents such as gentamycin, amikacin, kanamycin, streptomycin, paromoycin, neomycin, netilmicin and tobramycin. Other suitable aminoglycosides include seldomycins, sisomycins, aurimycin, lividomycins, streptothricins, hybrimycins, coralinomycin, butirosin, strepomutins, nebramycins, tenebrimycins, ribostamycins, destomycins, trehalosamines, myomycins, fortimicins, mutamicins and kasugamycin. Suitable aminoglycoside antibiotics are also disclosed in U.S. Patents Nos. 5,508,269; 4,645,760; and 4,380,625. It should be appreciated however that the present invention is not limited by any particular aminoglycoside antibiotic, and the invention is applicable to any aminoglycoside antibiotic now known or subsequently discovered or developed.

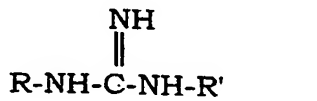
The aminoglycoside and substituted guanidine or other active compound may be administered simultaneously, in the same or different pharmaceutical formulations, or sequentially. Preferred the components of the combination of the invention are administered substantially simultaneously, e.g. in a unitary pharmaceutical composition containing the two components.

The invention also includes pharmaceutical compositions that comprise an aminoglycoside antibiotic in combination with a compound 2) such as a substituted guanidine or other compound as disclosed herein.

Other aspects of the invention are disclosed infra.

DETAILED DESCRIPTION OF THE INVENTION

Preferred compounds for use in combination with an aminoglycoside antibiotic include N,N'-disubstituted guanidines, including compounds of the following Formula I:



I

wherein R and R' each are an alkyl group of at least 4 carbon atoms or carbocyclic aryl groups of at least 6 carbon atoms, or heterocyclic or heteroaromatic of having 1 to 3 rings, 3 to 8 ring members in each and 1 to 3 heteroatoms, e.g., R and R', which can be the same or different, are alkyl of 4 or more carbon atoms, e.g., a 4 to 12 carbon atoms, preferably a straight chain, alkyl group and more preferably a 4 to 8 carbon atom alkyl group, for example, butyl, isobutyl, tertbutyl, amyl, hexyl, octyl, nonyl and decyl; cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, 1,4-methylenecyclohexane, adamantyl, cyclopentylmethyl, cyclohexylmethyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl or aralkyl, e.g., of up to 18 carbon atoms and containing 1-3 separate or fused aromatic rings, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-ethylphenyl and o-, m-, or p-propylphenyl, naphthyl, 2-naphthyl, and biphenyl, and heterocyclic aromatic rings including pyridyl, pyrazinyl, pyrimidyl, furyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, indolyl, and benzothiazolyl.

Additionally, 1, 2, 3 or more substituents may be present on the R and R' groups, e.g., alkyl of 1-8 carbon atoms, e.g., methyl, ethyl; halo, e.g., chloro, bromo, iodo, fluoro; nitro; azido; cyano; isocyanate; amino; lower-alkylamino; di-lower alkylamino; trifluoromethyl; alkoxy of 1-8 carbon atoms; e.g., methoxy, ethoxy and propoxy; acyloxy, e.g., alkanoyloxy of 1-8 carbon atoms, e.g., acetoxy and benzoxy; amido, e.g., acetamido, N-ethylacetamido; carbamido, e.g., carbamyl, N-methylcarbamyl, N,N'-dimethylcarbamyl; etc.

Especially preferred are compounds of Formula I wherein R and R' each are phenyl groups, which need not necessarily be identical, substituted with one or more of the foregoing substituents, for example, in the o-, m- or p-position or the o-, p- or m,m'-position, when the phenyl group is disubstituted, or R is phenyl or otherwise defined herein and R' is adamantyl.

Preferred compounds N,N'-disubstituted compounds for use in accordance with the invention include N,N'-di-m-tolylguanidine; N,N'-di-o-

iodophenylguanidine; N,N'-di-o-ethylphenylguanidine; N,N'-di-m-ethylphenylguanidine; N,N'-bis(2-iodophenyl)guanidine; N,N'-bis(3-tolyl)guanidine;N,N'-bis(3-ethylphenyl)guanidine; N,N'-bis(2-isopropylphenyl)guanidine; N,N'-bis(3-isopropylphenyl)guanidine; N,N'-bis(1-naphthyl)guanidine; N,N'-bis(3-methoxyphenyl)guanidine; N,N'-bis(3-trifluoromethylphenyl)guanidine; N,N'-bis(4-fluoro-3-ethylphenyl)guanidine; N,N'-bis(3,5-diethylphenyl)guanidine; N,N'-bis(3-nitrophenyl)guanidine; N,N'-bis(4-fluoro-3-nitrophenyl)guanidine; N,N'-bis(3-nitro-5-ethylphenyl)guanidine; N,N'-bis(3-azidophenyl)guanidine; N,N'-bis(quinolin-8-yl)guanidine; N,N'-bis(coumarin-8-yl)guanidine; N,N'-dibutylguanidine; N,N'-diphenylguanidine; N,N'-di-o-tolylguanidine; N,N'-di-(2-methyl-4-bromophenyl)guanidine; N,N'-di-(2-methyl-4-iodophenyl)guanidine; N,N'-di(cyclohexyl)guanidine; N,N'-di-(m-propylphenyl)guanidine; N,N'-di-(1-tetralinyl)guanidine; N,N'-di(±-endo-2-norbornyl)guanidine; N,N'-di-(exo-2-norbornyl)guanidine; N,N-di-(4-indanyl)guanidine; N,N'-diadamantylguanidine; and N,N'-dibenzylguanidine; and pharmaceutically acceptable salts of said compounds.

Asymmetrical N,N'-disubstituted guanidines are also preferred for use as compound 2) in methods and compositions of the invention, such as compounds of Formula I above wherein R and R' are different. Particularly preferred are asymmetrical compounds of Formula I wherein R and R' each are nonidentical aryl groups, including aryl groups substituted with one or more of the substituents discussed above with respect to Formula I, for example, in the o-, m- or p-position or the o-, p- or m,m'-position, when the phenyl group is disubstituted.

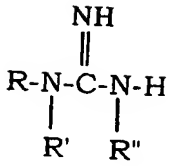
Especially preferred asymmetrical guanidines for use in the methods and compositions of the invention include N-(1-naphthyl)-N'-(o-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(m-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-methoxyphenyl)guanidine; N-(1-naphthyl)-N'-(4-indanyl)guanidine; N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-tolyl)guanidine; N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-methylphenyl)-N'-(m-

methoxyphenyl)guanidine; N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-tolyl)guanidine; N-(o-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(o-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-ethylphenyl)-N'-(4-indanyl)guanidine; N-(o-ethylphenyl)-N'-(m-ethylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-tolyl)guanidine; N-(o-iodophenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenylguanidine; N-(o-iodophenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-iodophenyl)-N'-(4-indanyl)guanidine; N-(o-iodophenyl)-N'-(o-ethylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(o-isopropylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(o-isopropylphenyl)-N'-(o-ethylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(m-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-isopropylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-methoxyphenyl)-N'-(m-tolyl)guanidine; N-(2,4-di-iodo-5-hydroxyphenyl)-N'-(2-tolyl)guanidine; N-(1-naphthyl)-N'-(2-iodophenyl)guanidine; N-(1-naphthyl)-N'-(3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(3-tolyl)guanidine; N-(1-naphthyl)-N-(4-bromo-3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-nitro-3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-[3-(1-hydroxy-ethyl)phenyl]guanidine; N-(4-fluoronaphthyl)-N'-(3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(1-naphthyl)-N'-(4-bromo-3-tolyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-tolyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(4-

indanyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-iodophenyl)guanidine; N-(1-naphthyl)N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(2-isopropylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(2-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-2-isopropylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-2-isopropylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(6-methoxy-4-fluoro-3-ethyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(7-fluoronaphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(coumarin-8-yl)-N-(3-ethylphenyl)guanidine; N-(coumarin-8-yl)-N'-(3-tolyl)guanidine; N-(quinolin-8-yl)-N'-(3-ethylphenyl)guanidine; N-(quinolin-8-yl)-N'-(3-tolyl)guanidine; N-(cyclohexyl)-N'-(4-bromo-2-methylphenyl)guanidine; N-(1-naphthyl)-N'-(o-iodophenyl)guanidine; N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(o-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-tolylphenyl)guanidine; N-(1-naphthyl)-N'-(o-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(m-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-methoxyphenyl)guanidine; N-(1-naphthyl)-N'-(4-indanylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(m-ethylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-tolylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-ethylphenyl)-N'-(4-indanylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-tolyl)guanidine; N-(o-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(o-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-

methoxyphenyl)guanidine; N-(o-ethylphenyl)-N'-(4-indanyl)guanidine; N-(o-iodophenyl)-N'-(m-tolyl)guanidine; N-(o-iodophenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-iodophenyl)-N'-(4-indanyl)guanidine; N-(o-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(o-isopropylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(m-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-methoxyphenyl)-N'-(m-tolyl)guanidine; N-(m-methoxyphenyl)-N'-(4-indanyl)guanidine; N-(4-indanyl)-N'-(m-tolyl)guanidine; N-(2-methylazidophenyl)-N'-(2-methylphenyl)guanidine; N-adamantyl-N'-(2-methylphenyl)guanidine; N-(iodophenyl)-N'-(2-methylphenyl)guanidine; N-(2-methyl-4-nitrophenyl)-N'-(2-methylphenyl)guanidine; N-(2-iodophenyl)-N'-(adamantyl)guanidine; N-(2-methylphenyl)-N'-(cyclohexyl)guanidine; N-adamantyl-N'-phenylguanidine; N-(3,5-dimethyl-1-adamantyl)-N'-(o-tolyl)guanidine; N-(3,5-dimethyl-1-adamantyl)-N'-(o-iodophenyl)guanidine; N-(1-adamantyl)-N'-(o-nitrophenyl)guanidine; N-(exo-2-isobornyl)-N'-(o-iodophenyl)guanidine; N-(exo-2-isobornyl)-N'-(o-tolyl)guanidine; N-(o-iodophenyl)-N'-(t-butyl)guanidine; N-(adamant-1-yl)-N'-(o-isopropylphenyl)guanidine; N-(adamant-1-yl)-N'-(p-bromo-o-tolyl)guanidine; N-(cyclohexyl)-N'-(p-bromo-o-tolyl)guanidine; N-(adamant-2-yl)-N'-(p-iodophenyl)guanidine; N-(adamantan-1-yl)-N'-(2-trifluoromethylphenyl)guanidine; N-(adamantan-1-yl)-N'-(2-methylphenyl)-N'-methylguanidine; N-(adamantan-1-yl)-N'-(6-coumarinyl)guanidine; N-(adamantan-1-yl)-N'-(8-coumarinyl)guanidine; N-(adamantan-1-yl)-N'-(2,4-difluorophenyl)guanidine; and N-(adamantan-1-yl)-N'-(2-trifluoromethyl-4-fluorophenyl)guanidine; and pharmaceutically acceptable salts of said compounds.

N,N,N'-trisubstituted guanidines are also preferred for use as compound 2) in the methods and compositions of the invention, including compounds of the following Formula II:



II

wherein R, R' and R" are independently a C_1-C_8 alkyl group, a C_2-C_8 alkenyl group, C_2-C_8 alkynyl group, cycloalkyl group, cycloalkyl group substituted by one or more substituents, cycloalkenyl group, cycloalkenyl group substituted with one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted by one or more substituents, alkaryl group, alkaryl group substituted by one or more substituents, heterocyclic group, heterocyclic group substituted by one or more substituents, heteroaryl group, or a heteroaryl group substituted by one or more substituents;

or a physiologically acceptable salt thereof;

wherein said substituent is a halogen of chloro, fluoro, bromo, iodo, C_1-C_8 alkyl, C_1-C_8 alkoxy, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_8 alkylthio, allyl, aralkyl, alkaryl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_8 acyl, aryl, heteroaryl, an aryl fused to a benzene ring, a heteroaryl fused to a benzene ring, C_3-C_6 heterocycloalkyl, a C_3-C_6 heterocycloalkyl ring fused to a benzene ring, C_1-C_8 alkylsulfonyl, arylthio, amino, C_1-C_8 alkylamino, C_2-C_{15} dialkylamino, hydroxy, hydroxyalkyl, carbamoyl, C_1-C_8 N-alkylcarbamoyl, C_2-C_{15} N,N'-dialkylcarbamoyl, nitro, azido or a C_2-C_{15} dialkylsulfamoyl.

Preferably, with reference to Formula II, preferred N,N,N'-trisubstituted guanidines are wherein R and R" are independently a cycloalkyl group, a cycloalkyl group substituted with one or more substituents, cycloalkenyl, cycloalkenyl substituted by one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted with one or more substituents, alkaryl group, alkaryl group substituted with one or more substituents, aralkyl group, aralkyl group substituted with one or more substituents, heterocyclic group, heterocyclic group substituted with one or more substituents, heteroaryl group, or a heteroaryl group substituted with one or more substituents; and R' is independently a C_1-C_8

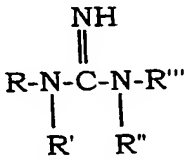
alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, an alkaryl group, or a substituted alkaryl group.

Especially preferred N,N,N'-trisubstituted guanidines for use as compound 2) in accordance with the invention include N,N'-di-(1-naphthyl)-N-methylguanidine; N,N'-di-(1-naphthyl)-N-ethylguanidine; N,N'-di-(m-ethylphenyl)-N-methylguanidine; N-(o-isopropylphenyl)-N'-methyl-N'-(1-naphthyl)guanidine; N-(m-ethylphenyl)-N-methyl-N'-(1-naphthyl)guanidine; N-ethyl-N,N'-di-(m-ethylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-ethyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N,N'-di-(m-ethylphenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-(isopropyl)-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-isopropyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-methyl-N-(4-indanyl)-N'-(m-

ethylphenyl)guanidine; N-methyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N-ethylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N'-methylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(2-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(5-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(8-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(6-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,4-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,6-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,4,6-trifluoro-3-ethylphenyl)-N'-methylguanidine; N-(2,4-difluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4-difluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4,5-trifluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4,8-trifluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(2,6-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(2,4-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(7-fluoro-1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(6-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N'-ethylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(4-fluoro-3-

ethylphenyl)-N'-methylguanidine; N,N'-di(8-coumarinyl)-N-methylguanidine; N,N'-di(8-coumarinyl)-N-ethylguanidine; N-(2-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(4-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(5-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(7-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4-difluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4,5-trifluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4,8-trifluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(5-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N'-ethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N'-ethylguanidine; and N-(8-coumarinyl)-N'-(3-trifluoromethylphenyl)-N'-ethylguanidine; and pharmaceutically acceptable salts of said compounds.

N,N,N',N'-tetrasubstituted guanidines are also preferred for use as compound 2) in accordance with the invention, including compounds of the following Formula III:



III

wherein R, R', R" and R"' are independently a C_1-C_8 alkyl group, a C_2-C_8 alkenyl group, C_2-C_8 alkynyl group, cycloalkyl group, cycloalkyl group substituted by one or more substituents, cycloalkenyl group, cycloalkenyl group substituted with one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted by one or more substituents, alkaryl group, alkaryl group substituted by one or more substituents, heterocyclic group, heterocyclic group substituted by one or more substituents,

heteroaryl group, or a heteroaryl group substituted by one or more substituents;

or a physiologically acceptable salt thereof;

wherein said substituent is halogen such as chloro, fluoro, bromo, iodo, C_1-C_8 alkyl, C_1-C_8 alkoxy, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_8 alkylthio, allyl, aralkyl, alkaryl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_8 acyl, aryl, heteroaryl, an aryl fused to a benzene ring, a heteroaryl fused to a benzene ring, C_3-C_6 heterocycloalkyl, a C_3-C_6 heterocycloalkyl ring fused to a benzene ring, C_1-C_8 alkylsulfonyl, arylthio, amino, C_1-C_8 alkylamino, C_2-C_{15} dialkylamino, hydroxy, hydroxyalkyl, carbamoyl, C_1-C_8 N-alkylcarbamoyl, C_2-C_{15} N,N'-dialkylcarbamoyl, nitro, azido or a C_2-C_{15} dialkylsulfamoyl.

With reference to Formula III, preferred N,N,N',N'-tetrasubstituted guanidines are wherein R and R" are independently a cycloalkyl group, a cycloalkyl group substituted with one or more substituents, a cycloalkyl group, a cycloalkyl group substituted with one or more substituents, a cycloalkenyl group, cycloalkenyl group substituted with one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted with one or more substituents, alkaryl group, alkaryl group substituted with one or more substituents, aralkyl group, aralkyl group substituted with one or more substituents, heterocyclic group, heterocyclic group substituted with one or more substituents, heteroaryl group, or a heteroaryl group substituted with one or more substituents; and R' and R"' are independently a C_1-C_8 alkyl group, C_2-C_6 alkenyl group, C_2-C_6 alkynyl group, an alkaryl group, a substituted alkaryl, a cycloalkaryl, or substituted cycloalkaryl group.

Especially preferred guanidines of Formula III are those wherein R and R" are independently carbocyclic aryl groups, substituted cycloalkyl groups, cycloalkenyl groups, cycloalkenyl groups substituted with one or more substituents, carbocyclic aryl groups, substituted carbocyclic aryl groups, alkaryl groups, substituted aralkyl groups, heterocyclic groups, substituted heterocyclic groups, heteroaryl groups, or substituted heteroaryl groups; and R' and R"' are C_1-C_8 alkyl groups. Particularly preferred N,N,N'N'-tetrasubstituted guanidines include N,N'-diethyl-N,N'-di-(m-

ethylphenyl)guanidine; N,N'-diethyl-N,N'-di-(1-naphthyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N,N'-diethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N,N'-dimethyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-ethyl-N'-isopropyl-N,N'-di-(m-ethylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-isopropylguanidine; N-ethyl-N-(4-indanyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(4-indenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N,N'-diisopropyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-

diisopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N,N'-diisopropyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl)-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N,N'-di-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-isopropylguanidine; N-methyl-N-(4-indanyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(4-indenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(1-naphthyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N,N'-di-(m-ethylphenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-methylguanidine; N,N'-di(1-naphthyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N,N-dimethylguanidine; N,N'-di(8-coumarinyl)-N,N'-dimethylguanidine; N,N'-di(8-coumarinyl)-N-methyl-N'-ethylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-

N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-azidophenyl)-N,N'-dimethylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-dimethylphenylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N-(3-methylphenyl)-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N,N'-diethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N,N'-diethylguanidine; N-(8-coumarinyl)-N'-(3-azidophenyl)-N,N'-diethylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-diethylphenylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N,N'-diethylguanidine; and N-(8-coumarinyl)-N-(3-methylphenyl)-N,N'-diethylguanidine; and pharmaceutically acceptable salts of said compounds.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical alkyl groups are, for example, methyl, ethyl, propyl, isopropyl, butyl, isobutyl, tert-butyl, amyl, hexyl, heptyl and octyl.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical cycloalkyl groups have 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cycloheptyl, 1,4-methylenecyclohexyl, adamantyl, norbornyl, isobornyl, menthyl, cyclopentylmethyl, cyclohexylmethyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical cycloalkenyl groups have 5 to 12 carbon atoms and include cyclopentenyl, cyclohexenyl, cycloheptenyl, and cyclooctenyl groups.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical carbocyclic

aryl groups include phenyl, 1-naphthyl, 2-naphthyl, biphenyl, phenanthracyl, and anthracyl groups.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical alkaryl or aralkyl groups, e.g., of up to 18 carbon atoms, may contain 1-3 separate or fused aromatic rings, e.g., benzyl, C_1-C_3 alkylphenyl, nitrophenyl, naphthyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl, o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m-ethylphenyl, o-propyl phenyl, and o-isopropylphenyl.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical heterocyclic aromatic rings include coumarinyl, pyridyl, pyrazinyl, pyrimidyl, furyl, pyrrolyl, thienyl, thiazolyl, oxazolyl, imidazolyl, indolyl, benzofuranyl and benzthiazolyl.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical alkenyl groups include allyl, 2-butenyl, 2-pentenyl and 2-hexenyl groups.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical alkynyl groups include 2-butynyl, 2-pentynyl and 2-hexynyl groups.

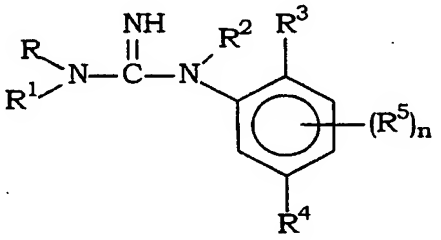
With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical aroyl groups include carbonyl substituted by the above-listed aryl groups.

With respect to the N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical aralkoxy groups include C_1-C_8 alkoxy groups substituted by the above-listed aryl groups.

With respect to N,N,N'-trisubstituted and N,N,N',N'-tetrasubstituted guanidines of Formulae II and III above, typical heterocycloalkyl groups include tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, morpholino and pyrrolidinyl groups.

Also preferred for use as compound 2) in accordance with the invention are substituted N,N'-disubstituted, N,N,N'-trisubstituted and

N,N,N',N'-tetrasubstituted guanidines having a 2,5-substituted-phenyl substituent, particularly compounds of the following Formula IV:



IV

wherein R, R^1 and R^2 are each independently hydrogen, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 carbon ring atoms, substituted or unsubstituted aralkyl having at least about 6 carbon ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R^3, R^4, and each R^5 substituent are each independently halogen, hydroxyl, azido, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or

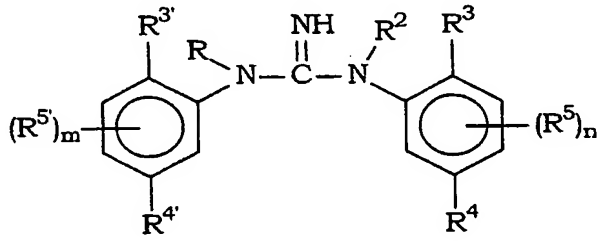
unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 carbon ring atoms, substituted or unsubstituted aralkyl having at least about 6 carbon ring atoms, nitro, cyano, substituted or unsubstituted alkanoyl such as C_{1-8} alkanoyl, e.g. acyl, or substituted or unsubstituted carboxy such as acid or ester groups of the formula $-(CH_2)_qCOOY$ where q is an integer of 0-8, Y is hydrogen or substituted or unsubstituted C_{1-8} alkyl; n is 0 (R^5 is hydrogen), 1, 2 or 3; or a pharmaceutically acceptable salt thereof.

In the above Formula IV, at least one of R and R^1 will typically be other than hydrogen. Preferred compounds of Formula IV include trisubstituted compounds where one of the guanidine substituents R, R^1 and R^2 of Formula IV above is hydrogen and the other two substituents are other than hydrogen, more preferably where R or R^1 is heterocyclic aryl or carbocyclic aryl, still more preferably where R is substituted or unsubstituted heterocyclic aryl or substituted or unsubstituted carbocyclic aryl and one of R^1 and R^2 is hydrogen and one of R^1 and R^2 is substituted or unsubstituted alkyl. Also preferred are N,N'-disubstituted compounds, i.e. where one of R and R^1 of Formula IV is hydrogen and R^2 is hydrogen, preferably where R is substituted or unsubstituted heterocyclic aryl or substituted or unsubstituted carbocyclic aryl and R^1 and R^2 are hydrogen. Also preferred are N,N,N'N'-tetrasubstituted compounds, i.e. where each of R, R^1 and R^2 substituents of Formula IV is other than hydrogen, preferably where R or R^1 is substituted or unsubstituted heterocyclic aryl or substituted or unsubstituted carbocyclic aryl, more preferably where R is substituted or unsubstituted heterocyclic aryl or substituted or unsubstituted carbocyclic aryl and R^1 and R^2 are each substituted or unsubstituted alkyl.

Preferred phenyl ring substituents R^3, R^4 and R^5 of compounds of Formula IV include halogen such as F, Cl, Br and I, hydroxyl, azido, substituted or unsubstituted alkyl including halogenated alkyl, substituted or unsubstituted alkoxy including halogenated alkoxy and substituted and unsubstituted alkylthio. Typically preferred phenyl ring substituents have 1 to 4 carbon atoms with methyl, ethyl and propyl including isopropyl being particularly preferred. Halogen-substituted alkyl and alkoxy groups are also

particularly preferred including fluoroalkyl having 1, 2, 3 or 4 carbon atoms such as trifluoromethyl and fluoro-substituted alkoxy having 1, 2, 3 or 4 carbon atoms such as trifluoromethoxy (-OCF_3). Methylthio (-SCH_3) and ethylthio (-SCH_2CH_3) are also particularly preferred phenyl ring substituents.

Particularly preferred R and R^1 groups of Formula IV include phenyl substituted at least at the 2,5 ring positions. For example, preferred are the following compounds of Formula IVa:

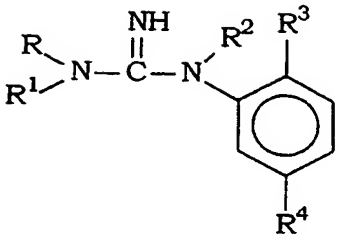


IVa

wherein R and R^2 are the same as defined above for Formula IV; each R^3, R^4, R^5, $R^{3'}$, $R^{4'}$ and $R^{5'}$ substituent is independently selected from the same group of substituents as defined above for R^3-R^5 of Formula IV; m and n are each independently 0 (R^5 and $R^{5'}$ are hydrogen when m and n are respectively 0), 1, 2 or 3; and pharmaceutically acceptable salts thereof. Preferred compounds of Formula IVa include those compounds where at least one of R and R^2 is other than heterocyclic aryl or carbocyclic aryl, e.g. where at least one of R and R^2 is hydrogen or substituted or unsubstituted alkyl, particularly substituted or unsubstituted alkyl having 1, 2, 3 or 4 carbon atoms. Preferred values of m and n of Formula IVa are 0 and 1.

Further preferred compounds of Formula IV include those compounds where the value n equals 1, particularly where n equals 1 and the phenyl ring is substituted by a R^5 group at the 3- or 4-position, i.e. the phenyl ring is 2,3,5-substituted or 2,4,5-substituted.

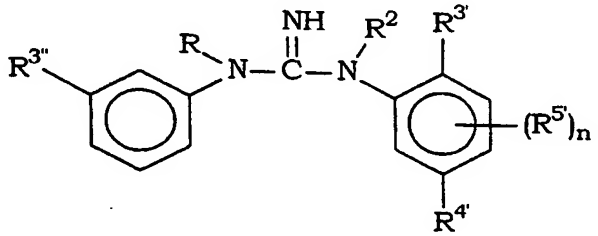
Especially preferred compounds of Formula IV are those where n is equal to zero (i.e., the 3, 4 and 6 positions of the phenyl ring are hydrogen-substituted), specifically compounds of the following Formula IVb:



IVb

where the groups R through R^4 are the same as specified above for Formula IV; and pharmaceutically acceptable salts thereof. Particularly preferred compounds of Formula IVb include those compounds where R is substituted or unsubstituted heterocyclic aryl or substituted or unsubstituted carbocyclic aryl such as substituted or unsubstituted phenyl or naphthyl and where at least one of R^1 and R^2 is other than heterocyclic aryl or carbocyclic aryl, e.g. where at least one of R^1 and R^2 is hydrogen or substituted or unsubstituted alkyl, particularly substituted or unsubstituted alkyl having 1, 2, 3 or 4 carbon atoms.

A still further group of preferred compounds 2) for use in accordance with the invention have, in addition to a 2,5-substituted phenyl moiety, at least one guanidine substituent (i.e., R, R^1 or R^2 of Formula IV) that is a phenyl group substituted at the 3-position, preferably without substitution at other ring positions. Particularly preferred are N-(3-substituted phenyl)-N'-(2,5-disubstituted phenyl)guanidines of the following Formula IVc:



IVc

wherein R, R^2 and n are the same as defined above for Formula IV; each $R^{3'}$, $R^{4'}$, $R^{5'}$ and $R^{3''}$ substituent is independently selected from the same group of substituents as defined above for R^3, R^4 and R^5 for Formula IV; and pharmaceutically salts of said compounds. Preferred compounds of Formula IVc include those compounds where at least one of R and R^2 is

other than heterocyclic aryl or carbocyclic aryl, e.g. where at least one of R and R^2 is hydrogen or substituted or unsubstituted alkyl, particularly substituted or unsubstituted alkyl having 1 to about 4 carbon atoms. Especially preferred are compounds of Formula IVc are those where one of R and R^2 is hydrogen and the other is substituted or unsubstituted alkyl having 1, 2, 3 or 4 carbon atoms, more preferably where R is methyl, ethyl or propyl and R^2 is hydrogen. Preferred values of n of Formula IVc are 0 and 1.

Specifically preferred compounds of Formula IV for use in the present methods include N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,5-dichlorophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-trifluromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-fluoro-5-trifluromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-fluoro-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-methylphenyl); N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-

ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-methylthio)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-methylthio)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(1-naphthyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2-fluoro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,4,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,4,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,3,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,3,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,4,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,3,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dichlorophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dimethylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-5-dimethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)-N-methylguanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-chloro-5-thiomethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-fluoro-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-thiomethyl-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-methoxy-5-methylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-methyl-N'-(2-chloro-5-thiomethylphenyl)guanidine; N-(8-quinolinyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(8-quinolinyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(8-quinolinyl)-N'-methyl-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-

methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl-N'-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-

(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-iodophenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-iodophenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-iodophenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-

ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-

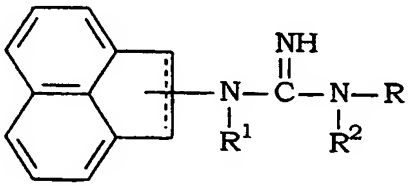
N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-iodo-5-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylsulfonylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfonylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfinylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfinylphenyl)-N'-(2,5-dibromophenyl)guanidine; and pharmaceutically acceptable salts of said compounds.

Preferred compounds of the above Formulae I through III also include those having a substituent of carbocyclic aryl with at least 6 ring carbons, particularly phenyl, and substituted at one or more ring positions by haloalkyl, substituted or unsubstituted thioalkyl having from 1 to about 3 carbon atoms, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl and haloalkyl. Specifically preferred compounds include N-(1-naphthyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfinylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfonylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N'-(3-

methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylthiophenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfinylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylsulfinylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfinylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfonylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylsulfonylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfonylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylthiophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-(3-pentafluoroethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-

methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(3-methylthiophenyl)-N-methyl-N'-(3-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-bromophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-bromophenyl)-N'-methylguanidine; N-(3-methylthiophenyl)-N-methyl-N'-(3-bromophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(3-bromophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl(3-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N,N'-dimethylguanidine; and pharmaceutically acceptable salts thereof.

Guanidine compounds having an acenaphthyl or acenaphthylene substituent are also preferred for use as a compound 2) in accordance with the invention, include compounds of the following Formula V:



V

wherein R is cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, 1,4-methylenecyclohexyl, 1- or 2-adamantyl, exo or endo 2-norbornyl, exo or endo 2-isobornyl, menthyl, cyclopentylmethyl, cyclohexylmethyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl, aralkyl or heterocyclic, e.g., of 6 to 18 carbon atoms and containing 1-3 separate or fused rings, and 0-5 O, N and/or S ring atoms in an aryl, alicyclic or mixed ring system, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-ethylphenyl and o-propylphenyl, 1-naphthyl, 2-naphthyl, biphenyl; indanyl, for example, 4-indanyl; indenyl, for example, 1- or 4-indenyl; 3-acenaphthyl, 5-acenaphthyl; 3-acenaphthylene, 5-

acenaphthylene; indolyl, for example, 7-indolyl; benzthiazole, quinolinyl, isoquinolinyl, pyridyl, pyrimidinyl, pyrazinyl, furanyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, coumarinyl, or imidazolyl;

R^1 and R^2 are the same or different and selected from the group consisting of hydrogen, lower C_{1-6} alkyl, lower C_{1-6} alkylamino, C_{5-10} aryl or substituted aryl;

wherein R and the acenaphthyl group are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkylamino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido.

Particularly preferred compounds within the scope of general Formula V include N,N'-di-(1-acenaphthyl)guanidine; N,N'-di-(3-acenaphthyl)guanidine; N,N'-di-(5-acenaphthyl)guanidine; N,N'-di-(acenaphthylen-1-yl)guanidine; N-(adamantan-1-yl)-N'-(5-acenaphthyl)guanidine; N-(adamantan-2-yl)-N-(5-acenaphthyl)guanidine; N-(adamantan-1-yl)-N-(3-acenaphthyl)guanidine; N-(adamantan-2-yl)-N'-(3-acenaphthyl)guanidine; N-(adamant-1-yl)-N'-(adamant-2-yl)guanidine; N-(3-acenaphthyl)-N'-(4-fluoronaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-fluoronaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-hydroxynaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-hydroxynaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-methoxynaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-methoxynaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-nitronaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-nitronaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-aminonaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-aminonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-azidonaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-azidonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-bromonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-bromonaphthyl)guanidine; N-(3-acenaphthyl)-N-(4-cyanonaphthyl)guanidine; N-(5-acenaphthyl)-N-(4-cyanonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-amidonaphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-amidonaphthyl)guanidine; N-(3-acenaphthyl)-(4-iodonaphthyl)guanidine; N-(5-acenaphthyl)-(4-iodonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(7-fluoronaphthyl)guanidine; N-(5-acenaphthyl)-N'-(7-

fluoronaphthyl)guanidine; N-(3-acenaphthyl)-N'-(2-fluoronaphthyl)guanidine; N-(5-acenaphthyl)-N'-(2-fluoronaphthyl)guanidine; N-(3-acenaphthyl)-N'-(2-methoxynaphthyl)guanidine; N-(5-acenaphthyl)-N'-(2-methoxynaphthyl)guanidine; N-(3-acenaphthyl)-N'-(2-hydroxynaphthyl)guanidine; N-(5-acenaphthyl)-N'-(2-hydroxynaphthyl)guanidine; N-(3-acenaphthyl)-N'-(2-aminonaphthyl)guanidine; N-(5-acenaphthyl)-N'-(2-aminonaphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-isopropylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-isopropylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-n-propylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-n-propylphenyl)guanidine; N-(3-acenaphthyl)-N-(2-isopropylphenyl)guanidine; N-(5-acenaphthyl)-N-(2-isopropylphenyl)guanidine; N-(3-acenaphthyl)-N-(4-cyclopropylphenyl)guanidine; N-(5-acenaphthyl)-N-(4-cyclopropylphenyl)guanidine; N-(3-acenaphthyl)-N'-(coumarinyl)guanidine; N-(5-acenaphthyl)-N'-(coumarinyl)guanidine; N-(3-acenaphthyl)-N'-(quinolinyl)guanidine; N-(5-acenaphthyl)-N'-(quinolinyl)guanidine; N-(4-hydroxy-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-hydroxy-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-hydroxy-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-hydroxy-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-nitro-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-nitro-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-amino-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-amino-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-amino-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-amino-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-methoxy-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-methoxy-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-methoxy-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-methoxy-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-bromo-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-bromo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(4-bromo-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(4-bromo-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-oxo-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-oxo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-

oxo-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-oxo-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-oxo-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(2-oxo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-oxo-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(2-oxo-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-bromo-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-bromo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-bromo-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-bromo-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-bromo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-bromo-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-bromo-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(2-bromo-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-hydroxy-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-hydroxy-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(1-hydroxy-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(1-hydroxy-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-hydroxy-3-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(2-hydroxy-3-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(2-hydroxy-5-acenaphthyl)-N'-(adamant-1-yl)guanidine; N-(2-hydroxy-5-acenaphthyl)-N'-(adamant-2-yl)guanidine; N-(3-acenaphthylenyl)-N'-(adamant-1-yl)guanidine; N-(3-acenaphthylenyl)-N'-(adamant-2-yl)guanidine; N-(5-acenaphthylenyl)-N'-(adamant-1-yl)guanidine; N-(5-acenaphthylenyl)-N'-(adamant-2-yl)guanidine; N,N'-bis(4-bromo-3-acenaphthyl)guanidine; N,N'-bis(4-bromo-5-acenaphthyl)guanidine; N,N'-bis(4-hydroxy-3-acenaphthyl)guanidine; N,N'-bis(4-hydroxy-5-acenaphthyl)guanidine; N,N'-bis(4-amino-3-acenaphthyl)guanidine; N,N'-bis(4-amino-5-acenaphthyl)guanidine; N,N'-bis(4-nitro-3-acenaphthyl)guanidine; N,N'-bis(4-nitro-5-acenaphthyl)guanidine; N,N'-bis(1-bromo-3-acenaphthyl)guanidine; N,N'-bis(1-bromo-5-acenaphthyl)guanidine; N,N'-bis(2-bromo-3-acenaphthyl)guanidine; N,N'-bis(2-bromo-5-acenaphthyl)guanidine; N,N'-bis(1-hydroxy-3-acenaphthyl)guanidine; N,N'-bis(1-hydroxy-5-acenaphthyl)guanidine; N,N'-bis(2-hydroxy-3-acenaphthyl)guanidine; N,N'-bis(2-hydroxy-5-acenaphthyl)guanidine; N,N'-bis(1-oxo-3-acenaphthyl)guanidine; N,N'-bis(1-oxo-5-acenaphthyl)guanidine; N,N'-bis(2-oxo-3-acenaphthyl)guanidine; N,N'-bis(2-oxo-5-acenaphthyl)guanidine; N,N'-bis(3-acenaphthylenyl)guanidine; N,N'-bis(4-azido-5-acenaphthyl)guanidine;

N,N'-bis(4-sulfonyl-5-acenaphthyl)guanidine; N,N'-bis(5-acenaphthylenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3,4-trichlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-bis-methylguanidine; N,N'-bis(5-acenaphthyl)-N-methylguanidine; N,N'-bis(5-acenaphthyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(1-anthracenyl)guanidine;N-(5-acenaphthyl)-N'-(1-anthracenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(1-anthracenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(1-anthracenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-tert-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-tert-butylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-tert-butylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-tert-butylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-cyclohexylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-cyclohexylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-cyclohexylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-cyclohexylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-sec-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-sec-butylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-sec-butylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-sec-butylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-methoxyphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxyphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxyphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dichlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3-dichlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dichlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dichlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-2-naphthyl)guanidine; N-(5-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-dichlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(3,4-dichlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-dichlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-

dichlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-chlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(4-chlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-chlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-chlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2-naphthyl)guanidine; N-(5-acenaphthyl)-N'-(2-naphthyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2-naphthyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2-naphthyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(6-quinolinyl)guanidine; N-(5-acenaphthyl)-N'-(6-quinolinyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(6-quinolinyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(6-quinolinyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-nitrophenyl)guanidine; N-(5-acenaphthyl)-N'-(4-nitrophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-nitrophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-nitrophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl-N'-(3-bi-phenyl)guanidine; N-(5-acenaphthyl-N'-(3-bi-phenyl)-N-methylguanidine; N-(5-acenaphthyl-N'-(3-bi-phenyl)-N'-methylguanidine; N-(5-acenaphthyl-N'-(3-bi-phenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dimethylphenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3-dimethylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dimethylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,3-dimethylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2-bi-phenyl)guanidine; N-(5-acenaphthyl)-N'-(2-bi-phenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2-bi-phenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2-bi-phenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2,5-dibromophenyl)guanidine; N-(5-acenaphthyl)-N'-(2,5-dibromophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,5-dibromophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-dimethoxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(4-chloro-1-naphthyl)guanidine; N-

(5-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3,4,5-trichlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-bi-phenyl)guanidine; N-(5-acenaphthyl)-N'-(4-bi-phenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-bi-phenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-bi-phenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-isopropylphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-isopropylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-isopropylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-isopropylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-tert-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-tert-butylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-tert-butylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-tert-butylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)guanidine; N-(5-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-iodophenyl)guanidine; N-(5-acenaphthyl)-N'-(3-iodophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-iodophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-iodophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-nitrophenyl)guanidine; N-(5-acenaphthyl)-N'-(3-nitrophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-nitrophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(5-indolinyl)guanidine; N-(5-acenaphthyl)-N'-(5-indolinyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(5-indolinyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(5-indolinyl)-N,N'-bis-

methylguanidine; N-(5-acenaphthyl)-N'-(3-acenaphthyl)guanidine; N-(5-acenaphthyl)-N'-(3-acenaphthyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-acenaphthyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-acenaphthyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(2-fluorenyl)guanidine; N-(5-acenaphthyl)-N'-(2-fluorenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2-fluorenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(2-fluorenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-n-butoxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-n-butoxyphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-n-butoxyphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-n-butoxyphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)guanidine; N-(5-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)guanidine; N-(5-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-trifluoromethylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-methylthiophenyl)guanidine; N-(5-acenaphthyl)-N'-(4-methylthiophenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(4-methylthiophenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-methylthiophenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(3-sec-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-sec-butylphenyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(3-sec-butylphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-sec-butylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-bis-methylguanidine; N,N'-bis(3-acenaphthyl)-N-methylguanidine; N,N'-bis(3-acenaphthyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(1-anthracenyl)guanidine; N-(3-

acenaphthyl)-N'-(1-anthracenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(1-anthracenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(1-anthracenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-tert-butylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-tert-butylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-tert-butylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-tert-butylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-cyclohexylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-cyclohexylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-cyclohexylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-cyclohexylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-sec-butylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-sec-butylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-sec-butylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-sec-butylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-methoxyphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxyphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxyphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dichlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3-dichlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dichlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dichlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-2-naphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-2-naphthyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dichlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(3,4-dichlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dichlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dichlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-chlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(4-chlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-chlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-chlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2-naphthyl)guanidine; N-(3-acenaphthyl)-N'-(2-naphthyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2-naphthyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2-naphthyl)-N,N'-bis-

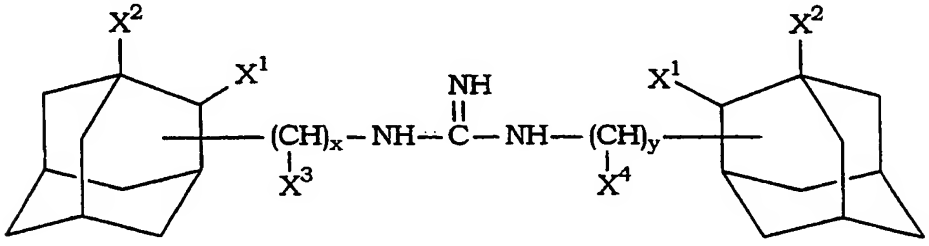
methylguanidine; N-(3-acenaphthyl)-N'-(6-quinolinyl)guanidine; N-(3-acenaphthyl)-N'-(6-quinolinyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(6-quinolinyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(6-quinolinyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-nitrophenyl)guanidine; N-(3-acenaphthyl)-N'-(4-nitrophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-nitrophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-nitrophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl-N'-(3-bi-phenyl)guanidine; N-(3-acenaphthyl-N'-(3-bi-phenyl)-N-methylguanidine; N-(3-acenaphthyl-N'-(3-bi-phenyl)-N'-methylguanidine; N-(3-acenaphthyl-N'-(3-bi-phenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dimethylphenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3-dimethylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dimethylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,3-dimethylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2-bi-phenyl)guanidine; N-(3-acenaphthyl)-N'-(2-bi-phenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2-bi-phenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2-bi-phenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-acenaphthyl)-N'-(2,5-dibromophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,5-dibromophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dimethoxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3,4-dimethoxyphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-methoxy-1-naphthyl)-N,N'-dimethylguanidine; N-(3-acenaphthyl)-N'-(4-chloro-1-naphthyl)guanidine; N-(3-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-chloro-1-naphthyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3,4,5-trichlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3,4,5-trichlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-bi-

phenyl)guanidine; N-(3-acenaphthyl)-N'-(4-bi-phenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-bi-phenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-bi-phenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,4,5-tetrachlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-isopropylphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-isopropylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-isopropylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-isopropylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-tert-butylphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-tert-butylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-tert-butylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-tert-butylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2,3,5,6-tetrachlorophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-iodophenyl)guanidine; N-(3-acenaphthyl)-N'-(3-iodophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-iodophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-iodophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-nitrophenyl)guanidine; N-(3-acenaphthyl)-N'-(3-nitrophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-nitrophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(5-indolinyl)guanidine; N-(3-acenaphthyl)-N'-(5-indolinyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(5-indolinyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(5-indolinyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(2-fluorenyl)guanidine; N-(3-acenaphthyl)-N'-(2-fluorenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(2-fluorenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(2-fluorenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-n-butoxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-n-butoxyphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-n-butoxyphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-n-butoxyphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-(2-

methoxy)dibenzofuranyl)guanidine; N-(3-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-(2-methoxy)dibenzofuranyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)guanidine; N-(3-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(9-hydroxy-2-fluorenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-trifluoromethylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-trifluoromethylphenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(4-methylthiophenyl)guanidine; N-(3-acenaphthyl)-N'-(4-methylthiophenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(4-methylthiophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-methylthiophenyl)-N,N'-bis-methylguanidine; N-(3-acenaphthyl)-N'-(3-sec-butylphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-sec-butylphenyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(3-sec-butylphenyl)-N'-methylguanidine; N-(3-acenaphthyl); N'-(3-sec-butylphenyl)-N,N'-bis-methylguanidine; N-(5-acenaphthyl)-N'-(4-benzyloxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-benzyloxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-sec-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(2-anthracenyl)guanidine; N-(5-acenaphthyl)-N'-(3-phenethylphenyl)guanidine; N-(5-acenaphthyl)-N'-(4-adamantylphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-benzyloxyphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-benzyloxyphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-biphenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(3-(1'-methyl-2'-phenylethyl)phenyl)guanidine; N-(5-acenaphthyl)-N'-(3,4-tetralinylphenyl)guanidine; N-(5-acenaphthyl)-N'-(7-benzyltetralinylphenyl)guanidine; N-(5-acenaphthyl)-N'-(3,4-dibenzyloxyphenyl)guanidine; N-(5-acenaphthyl)-N'-(3-1-(4-ethoxy)phenyl)propanyl)phenyl)guanidine; N-(5-acenaphthyl)-N'-(3-(N',N'-dibenzyl)aminophenyl)guanidine; N-(5-acenaphthyl)-N'-(3-(1'-benzylbutyl)phenyl)guanidine; N-(5-acenaphthyl)-N'-3-(4-tert-butylbenzoxymethyl)phenylguanidine; N-(5-acenaphthyl)-N'-(2-(2-indolyl)phenyl)guanidine; N-(5-acenaphthyl-N'-(3-bromophenyl)guanidine;

N-(5-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(2,3,4-trichloro-phenyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(4-(2'-benzothiazole-6'-methyl)phenyl)guanidine; N-(3-acenaphthyl)-N'-(4-benzoyloxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-benzoyloxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-sec-butylphenyl)guanidine; N-(3-acenaphthyl)-N'-(2-anthracenyl)guanidine; N-(3-acenaphthyl)-N'-(3-phenethylphenyl)guanidine; N-(3-acenaphthyl)-N'-(4-adamantylphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-benzyloxyphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-benzyloxyphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-biphenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(3-(1'-methyl-2'-phenylethyl)phenyl)guanidine; N-(3-acenaphthyl)-N'-(3,4-tetralinylphenyl)guanidine; N-(3-acenaphthyl)-N'-(7-benzyltetralinylphenyl)guanidine; N-(3-acenaphthyl)-N'-(3-1-(4-ethoxy)phenyl)propanyl)phenyl)guanidine; N-(3-acenaphthyl)-N'-(3-(N",N"-dibenzyl)aminophenyl)guanidine; N-(3-acenaphthyl)-N'-(3-(1'-benzylbutyl)phenyl)guanidine; N-(3-acenaphthyl)-N'-3-(4-tert-butylbenzoxymethyl)phenylguanidine; N-(3-acenaphthyl)-N'-(2-(2-indolyl)phenyl)guanidine; N-(3-acenaphthyl-N'-(3-bromophenyl)guanidine; N-(3-acenaphthyl)-N'-(3,4-dibenzyloxyphenyl)guanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine; N-(3-acenaphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(4-(2'-benzothiazole-6'-methylphenyl)guanidine; and pharmaceutically acceptable salts of said compounds.

Another preferred group of compounds for use as a compound 2) in accordance with the invention is diadamantylguanidine compounds of the following Formula VI:

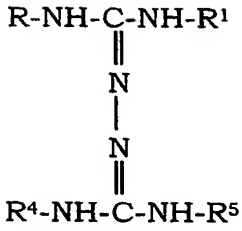


VI

wherein X^1, X^2, X^3, and X^4 are the same or different and are selected from the group consisting of hydrogen, hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocynato, halogen, amido, sulfonato or carbamido; wherein at least one of X^1, X^2, X^3, and X^4 is other than hydrogen; x and y are the same or different and are 0, 1, 2, 3 or 4.

Specifically preferred diadamantyl guanidines for use in the present methods include di-(3-nitroadamantan-1-yl)guanidine; N,N'-di-(3-hydroxyadamantan-1-yl)guanidine, N,N'-di-(3-amino-adamantan-1-yl)guanidine; N,N'-di-(3-nitro-adamantan-2-yl)guanidine; N,N'-di-(3-hydroxyadamantan-2-yl)guanidine; N,N'-di-(3-aminoadamantan-2-yl)guanidine; N,N'-di-(5-nitroadamantan-2-yl)guanidine; N,N'-di-(5-hydroxy-adamantan-2-yl)guanidine; N,N'-di-(5-aminoadamantan-2-yl)guanidine; N,N'-di-(methylene-adamantan-1-yl)guanidine; N,N'-di-(methylene-adamantan-2-yl)guanidine; N-(adamantan-1-yl)-N'-(methyleneadamantan-1-yl)guanidine; N-(adamantan-2-yl)-N'-(methyleneadamantan-2-yl)guanidine; N-(adamantan-1-yl)-N'-(methyleneadamantan-2-yl)guanidine; N-(adamantan-2-yl)-N'-(methyleneadamantan-1-yl)guanidine; N,N'-di-(methylene-(3-aminoadamantan-1-yl))guanidine; N,N'-di-(methylene-(3-aminoadamantan-2-yl))guanidine; N,N'-di-(methylene-(3-hydroxyadamantan-1-yl))guanidine; N,N'-di-(methylene-(3-hydroxyadamantan-2-yl))guanidine; N,N'-di-(methylene-(3-mercaptoadamantan-1-yl))guanidine; N,N'-di-(methylene-(3-mercapto-adamantan-2-yl))guanidine; N,N'-di-(methylene-(3-mercaptoadamantan-1-yl))guanidine; N,N'-di-(methylene-(3-mercaptoadamantan-2-yl))guanidine; N,N'-di-(methylene-(3-cyanoadamantan-1-yl))guanidine; N,N'-di-(methylene-(3-cyanoadamantan-2-yl))guanidine; N,N'-di-(methylene-(3-cyanoadamantan-1-yl))guanidine; and N,N'-di-(methylene-(3-cyanoadamantan-2-yl))guanidine; and pharmaceutically acceptable salts thereof.

A further preferred group of compounds for use as a compound 2) in accordance with the invention is hydrazinedicarboximidamide compounds of the following Formula VII:



VII

or a tautomer thereof,

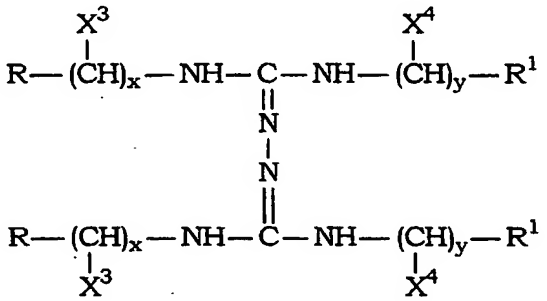
wherein R, R^1, R^4 and R^5 are the same or different and are cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, 1,4-methylenecyclohexyl, 1- or 2-adamantyl, exo or endo 2-norbornyl, exo or endo 2-isobornyl, menthyl, cyclopentyl-methyl, cyclohexylmethyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl, aralkyl or heterocyclic, e.g., of 6 to 18 carbon atoms and containing 1-3 separate or fused rings, and 0-5 O, N and/or S ring atoms in an aryl, alicyclic or mixed ring system, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-ethylphenyl and o-propylphenyl, 1-naphthyl, 2-naphthyl, biphenyl; indanyl, for example, 4-indanyl; indenyl, for example, 1- or 4-indenyl; 3-acenaphthyl, 5-acenaphthyl; 3-acenaphthylene, 5-acenaphthylene; indolyl, for example, 7-indolyl; benzthiazole, quinolinyl, isoquinolinyl, pyridyl, pyrimidinyl, pyrazinyl, furanyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, coumarinyl; or imidazolyl;

wherein R, R^1, R^4 or R^5 is optionally substituted hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido.

Specifically preferred compounds of Formula VII for use in accordance with the invention include N,N',N",N"'-tetracyclohexylhydrazinedicarboximidamide; N,N',N",N"'-tetraphenylhydrazinedicarboximidamide; N,N'-di-(adamantan-1-yl)-N",N"'-dicyclohexylhydrazinedicarboximidamide; N,N',N",N"'-tetra-(adamantan-1-yl)hydrazinedicarboximidamide; N,N',N",N"'-tetra-(adamantan-2-yl)-hydrazinedicarboximidamide; N,N'-di-(adamantan-1-yl)-N",N"'-di-

(adamantan-2-yl)-hydrazinedicarboximidamide; N,N'-di-(2-norbornyl)-N",N"'-dicyclohexylhydrazinedicarboximidamide; N,N'-di-(2-isobornyl)-N",N"'-dicyclohexylhydrazinedicarboximidamide; N,N'-di-(2-isobornyl)-N",N"'-di-(adamantan-1-yl)hydrazinedicarboximidamide; N,N'-di-(2-isobornyl)-N",N"'-di-(adamantan-2-yl)hydrazinedicarboximidamide; N,N',N",N"'-tetra-(acenaphth-5-yl)hydrazinedicarboximidamide; N,N',N",N"'-tetra-(acenaphthylen-5-yl)-hydrazinedicarboximidamide; N,N'-di-(acenaphth-5-yl)-N",N"'-di-(acenaphthylen-5-yl)-hydrazinedicarboximidamide; N,N'-di-(2-norbornyl)-N",N"'-di-(acenaphth-5-yl)hydrazinedicarboximidamide; N,N'-di-(2-norbornyl)-N",N"'-di-(acenaphthylen-5-yl)hydrazinedicarboximidamide; N,N'-di-(2-isobornyl)-N",N"'-di-(acenaphth-5-yl)hydrazinedicarboximidamide; N,N'-di-(2-isobornyl)-N",N"'-di-(acenaphthylen-5-yl)hydrazinedicarboximidamide; N,N'-dicyclohexyl-N",N"'-di-(acenaphth-5-yl)hydrazinedicarboximidamide; and N,N'-dicyclohexyl-N",N"'-di-(acenaphthylen-5-yl)hydrazinedicarboximidamide.

Also preferred for use as a compound 2) in accordance with the invention are hydrazinecarboximidamides of the following Formula VIII:



VIII

or a tautomer thereof;

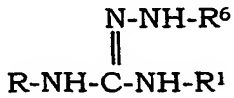
wherein R and R^1 are the same or different and are cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, 1,4-methylenecyclohexyl, 1- or 2-adamantyl, exo or endo 2-norbornyl, exo or endo 2-isobornyl, menthyl, cyclopentyl-methyl, cyclohexyl-methyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl, aralkyl or heterocyclic, e.g., of 6 to 18 carbon atoms and containing 1-3 separate or fused rings, and 0-5 O, N and/or S ring atoms in

an aryl, alicyclic or mixed ring system, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-ethylphenyl and o-propylphenyl, 1-naphthyl, 2-naphthyl, biphenyl; indanyl, for example, 4-indanyl; 3-acenaphthyl, 5-acenaphthyl; 3-acenaphthylene, 5-acenaphthylene; indenyl, for example, 1- or 4-indenyl; indolyl, for example, 7-indolyl; benzthiazole; quinolinyl; isoquinolinyl; pyridyl; pyrimidinyl, pyrazinyl; furanyl, thienyl, pyrrolyl; thiazolyl, oxazolyl, coumarinyl, or imidazolyl;

X^3 and X^4 are the same or different and are selected from the group consisting of hydrogen, hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino; alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato, or carbamido;

wherein R and R^1 are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido; x and y are the same or different and are 0, 1, 2, 3 or 4.

Also preferred for use as a compound 2) in accordance with the invention are aminoguanidines, including compounds of the following Formula IX:



IX

or a tautomer thereof,

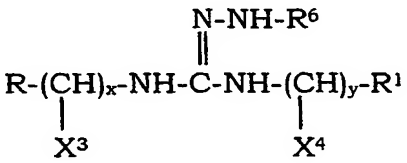
wherein R and R^1 are the same or different and are cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, 1,4-methylenecyclohexyl, 1- or 2-adamantyl, exo or endo 2-norbornyl, exo or endo 2-isobornyl, menthyl, cyclopentyl-methyl, cyclohexyl-methyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl, aralkyl or heterocyclic, e.g., of 6 to 18 carbon atoms and containing 1-3 separate or fused rings, and 0-5 O, N and/or S ring atoms in

an aryl, alicyclic or mixed ring system, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-ethylphenyl and o-propylphenyl, 1-naphthyl, 2-naphthyl, biphenyl; indanyl, for example, 4-indanyl; indenyl, for example, 1- or 4-indenyl; 3-acenaphthyl, 5-acenaphthyl; 3-acenaphthylene, 5-acenaphthylene; indolyl, for example, 7-indolyl; benzthiazole, quinolinyl, isoquinolinyl, pyridyl, pyrimidinyl, pyrazinyl, furanyl, thienyl, pyrrolyl, thiazolyl; oxazolyl, coumarinyl, or imidazolyl;

wherein R and R^1 are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido;

R^6 is hydrogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, carbocyclic aryl, nitrile, C_1-C_6 alkoxycarbonyl, C_1-C_6 acyl or benzoyl.

Further preferred aminoguanidines for use as compound 2) in accordance with the invention are compounds of the following Formula X:



X

or a tautomer thereof,

wherein R and R^1 are the same or different and are cycloalkyl of 3 to 12 carbon atoms, e.g., cyclopropyl, cyclopentyl, cyclohexyl, cyclohexenyl, cycloheptyl, 1,4-methylenecyclohexyl, 1- or 2-adamantyl, exo or endo 2-norbornyl, exo or endo 2-isobornyl, menthyl, cyclopentyl-methyl, cyclohexyl-methyl, 1- or 2-cyclohexylethyl and 1-, 2- or 3-cyclohexylpropyl; carbocyclic aryl, alkaryl, aralkyl or heterocyclic, e.g., of 6 to 18 carbon atoms and containing 1-3 separate or fused rings, and 0-5 O, N and/or S ring atoms in an aryl, alicyclic or mixed ring system, e.g., phenyl, benzyl, 1- and 2-phenylethyl, 1-, 2-, or 3-phenylpropyl; o-, m-, or p-tolyl, m,m'-dimethylphenyl, o-, m-, or p-ethylphenyl, m,m'-diethylphenyl, m-methyl-m'-

ethylphenyl and o-propylphenyl, 1-naphthyl, 2-naphthyl, biphenyl; indanyl, for example, 4-indanyl; indenyl, for example, 1- or 4-indenyl; 3-acenaphthyl, 5-acenaphthyl; 3-acenaphthylene, 5-acenaphthylene; indolyl, for example, 7-indolyl; benzthiazole, quinolinyl, isoquinolinyl, pyridyl, pyrimidinyl, pyrazinyl, furanyl, thienyl, pyrrolyl, thiazolyl, oxazolyl, coumarinyl, or imidazolyl;

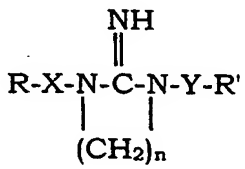
X^3 and X^4 are the same or different and selected from the group consisting of hydrogen, hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido;

wherein R and R^1 are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido;

x and y are the same or different and are 0, 1, 2, 3 or 4;

R^6 is hydrogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, carbocyclic aryl, nitrile, C_1-C_6 alkoxycarbonyl, C_1-C_6 acyl or benzoyl. Specifically preferred compounds of Formula X include N,N'-dicyclohexyl-N"-aminoguanidine, N,N'-di-(adamantan-1-yl)-N"-aminoguanidine, N,N'-di-(adamantan-2-yl)-N"-aminoguanidine, N,N'-di-(2-norbornyl)-N"-aminoguanidine, and N,N'-di-(2-isobornyl)-N"-aminoguanidine.

Also preferred for use as compound 2) in accordance with the invention are compounds of the following Formula XI:



XI

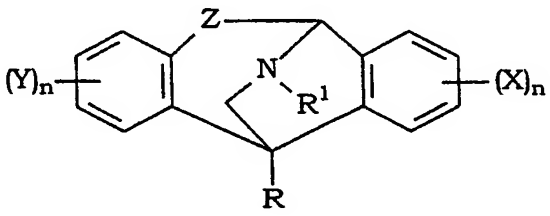
wherein

n is 2, 3, 4 or 5;

X and Y are independently a single bond, a branched or straight chain C_1-C_{12} alkylene or a branched or straight chain alkenylene;

R and R' are independently hydrogen, substituted or unsubstituted a cycloalkyl group of at least 3 carbons, a substituted or unsubstituted carbocyclic group of at least 6 carbon atoms, particularly substituted or unsubstituted phenyl; substituted or unsubstituted aralkyl of at least 6 carbon atoms and containing 1-3 separate or fused rings, or a substituted or unsubstituted heterocyclic or heteroaromatic group having from 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms, and wherein each of R and R' may be substituted; or wherein R and R' together with the guanidine nitrogen to which they are attached form a saturated or unsaturated cyclic ring containing at least 2 carbon atoms exclusive of the guanidine carbon atom, and wherein said cyclic ring may be substituted with one or more alkyl groups of 1-6 carbon atoms, carbocyclic aryl or at least 6 carbon atoms, cycloalkyl groups of 3-12 carbon atoms, or 1-2 fused aromatic rings; and pharmaceutically acceptable salts thereof. Specifically preferred compounds of Formula XI include N,N'-di(m-ethylphenyl)-2-iminodazolidine; N,N'-bis-(4-tert-butylphenyl)-2-iminopyrimidazolidine; N,N'-bis-(4-pentylphenyl)-2-iminopyrimidazolidine; N,N'-bis-(4-hexylphenyl)-2-iminopyrimidazolidine; N,N'-bis-(naphthyl)-2-iminopyrimidazolidine; N,N'-bis-(5-acenaphthyl)-2-iminopyrimidazolidine; N,N'-bis-(tetralinyl)-2-iminopyrimidazolidine.

A further group of compounds preferred for use as compound 2) in accordance with the invention are compounds of the following Formula XII:



XII

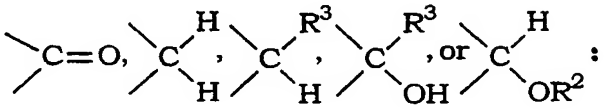
wherein:

R is hydrogen, C_2-C_6 acyl, C_1-C_6 alkyl, aryl, C_1-C_6 alkoxycarbonyl, C_7-C_{10} aralkyl, C_2-C_6 alkenyl, C_3-C_{15} dialkylaminoalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, C_3-C_{15} trialkylsilyl, C_4-C_{10} alkylcycloalkyl, or C_3-C_6 cycloalkyl;

R^1 hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_7-C_{10} aralkyl, C_1-C_6 alkoxy, C_1-C_6 alkylamino, or C_3-C_{15} dialkylaminoalkyl;

X and Y are independently selected from the group consisting of a halogen such as chloro, fluoro, bromo, iodo, C_1-C_6 alkoxy, C_2-C_6 dialkoxymethyl, C_1-C_6 alkyl, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_6 haloalkyl, e.g. trifluoromethyl; C_1-C_6 haloalkylthio, allyl, aralkyl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_6 acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, C_3-C_6 heterocycloalkyl, C_1-C_6 alkylthio, C_1-C_6 alkylsulfonyl, C_1-C_6 haloalkylsulfonyl, C_1-C_6 alkylsulfinyl, C_1-C_6 haloalkylsulfinyl, arylthio, C_1-C_6 haloalkoxy, amino, C_1-C_6 alkylamino, C_2-C_{15} dialkylamino, hydroxy, carbamoyl, C_1-C_6 N-alkylcarbamoyl, C_2-C_{15} N,N-dialkylcarbamoyl, nitro and C_2-C_{15} dialkylsulfamoyl;

Z represents a group selected from



wherein R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, aralkyl, C_4-C_{15} dialkylaminoalkyl, heterocycloalkyl, C_2-C_6 acyl, aroyl, or aralkanoyl, and R^3 is C_1-C_6 alkyl, C_2-C_6 alkenyl, phenyl, aralkyl or C_3-C_{15} dialkylaminoalkyl; and

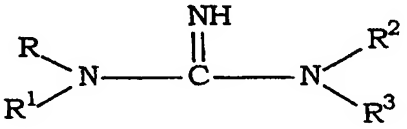
n is an integer selected from 0 (X or Y is hydrogen, respectively), 1, 2, 3 or 4, or a pharmaceutically acceptable salt thereof. The compounds having Formula (XII) above may exist in racemic form or in the optically active stereoisomeric form. With respect to Formula XII, typical C_1-C_6 alkyl groups include methyl, ethyl, n-propyl, i-propyl, n-butyl t-butyl, i-butyl, pentyl, i-pentyl and hexyl groups; typical C_2-C_6 acyl groups include acetyl, propanoyl, i-propanoyl, butanoyl, s-butanoyl, pentanoyl and hexanoyl; typical aryl groups include phenyl, naphthyl, phenanthryl and anthracyl; typical C_1-C_6 alkoxycarbonyl groups include carbonyl substituted by methoxy, ethoxy, propanoxy, i-propanoxy, n-butanoxy, t-butanoxy, i-butanoxy, petanoxy and hexanoxy; typical aralkyl groups include the above-listed C_1-C_6 alkyl groups substituted by phenyl, naphthyl, phenanthryl and

anthracyl groups, e.g. benzyl, phenethyl, phenylpropyl, phenylisopropyl and phenylbutyl; typical C_2-C_6 alkenyl groups include vinyl, allyl, 2-butenyl, 2-pentenyl and 2-hexenyl groups; typical C_2-C_6 alkynyl groups include ethynyl and proparyl groups; typical halo include fluoro, chloro, bromo and iodo; typical aroyl include carbonyl substituted by phenyl, naphthyl, phenanthryl and anthracyl; typical aralkanoyl groups include carbonyl substituted by the above-listed aralkyl groups; typical aralkoxy groups include the above-listed C_1-C_6 alkoxy groups substituted by phenyl, naphthyl, phenanthyl and anthracyl groups; typical substituted aryl groups include the above-listed aryl groups substituted by halo, hydroxy, amino and the like; typical heteroaryl groups include furyl, thienyl, pyrrolyl, thiazolyl, pyridyl, pyrimidinyl, pyrizinyl and oxazolyl; typical substituted heteroaryl groups include the above-listed heteroaryl groups substituted by halo, C_1-C_6 alkyl and the like; typical C_5-C_6 heterocycloalkyl groups include tetrahydrofuranyl, tetrahydropyranyl, piperidinyl and pyrrolidinyl; typical C_3-C_{15}-dialkylaminoalkyl groups include N,N-dimethylaminomethyl, N,N-dimethylaminoethyl, N,N-dimethylaminopropyl and N,N-dimethylaminobutyl.

Specifically preferred compounds of Formula XII for use in accordance with the invention are disclosed in PCT/US92/03554 and include (+) and/or (-) 10,5-(iminomethano)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene; (+) and/or (-) 5-methyl-10,5-(iminomethano)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene; (+) and/or (-) N-methyl-10,5-(iminomethano)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene; (+) and/or (-) 5-methyl-N-methyl-10,5-(iminomethano)-10,11-dihydro-5H-dibenzo[a,d]cycloheptene; (-)-3-chloro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (+) 3-chloro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (-)-N-methyl-3-chloro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (+)-N-methyl-3-chloro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-iodo-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; N-methyl-3-iodo-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 7-methoxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-bromo-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-

chloro-7-methoxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-bromo-7-methoxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 7-chloro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-amino-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-bromo-N-methyl-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-bromo-7-methoxy-N-methyl-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (-)-3-fluoro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (+)-3-fluoro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (-)-N-methyl-3-fluoro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; (+)-N-methyl-3-fluoro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-methoxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-nitro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-azido-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-trifluoromethyl-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; N-methyl-3-trifluoromethyl-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3,7-difluoro-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-phenyl-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-amino-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 8-hydroxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-hydroxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 8-methoxy-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; 3-cyano-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; and 3-methylthio-5-(iminomethano)-10,11-dihydro-5H-dibenzo-[a,d]cycloheptene; and pharmaceutically acceptable salts thereof. Racemic mixtures and optically active isomers of the above compounds are also preferred.

N,N-disubstituted guanidines are also preferred for use as compound 2) in accordance with the invention, including compounds of the following Formula XIII:



XIII

wherein:

R and R^1 are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 5 ring atoms, substituted or unsubstituted aralkyl having at least about 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 heteroatoms, with at least one of R and R^1 being carbocyclic aryl, aralkyl, a heteroaromatic group or a heterocyclic group;

R^2 and R^3 each being independently selected from the group consisting of hydrogen, substituted and unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted and unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, and substituted and unsubstituted aminoalkyl; and pharmaceutically acceptable salts thereof. A preferred group of compounds of Formula XIII are those wherein at least one and more preferably both of R^2 and R^3 are hydrogen, i.e. compounds of the formula $R(R^1)NC(=NH)NH_2$ where R and R^1 are as defined above for Formula XIII. Also preferred is where at least one, or more preferably both, of R and R^1 is substituted or unsubstituted carbocyclic aryl or substituted or unsubstituted aralkyl or substituted or unsubstituted alkaryl. Preferred compounds of Formula XIII also include those compounds having substituents with 1 to about 6 carbon atoms, particularly R^2 and/or R^3 groups that have 1 to 6 carbon atoms (where R^2 and/or R^3 are other than hydrogen). Particularly preferred R^2 and R^3

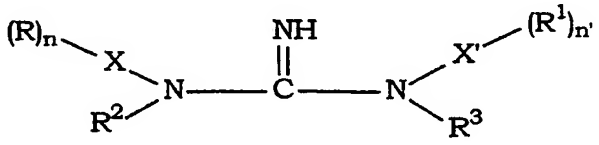
substituents of compounds of Formula XIII include unsubstituted alkyl and heteroalkyl such as alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl and aminoalkyl. Preferred R and R^1 groups include substituted and unsubstituted acenaphthyl, phenyl, biphenyl, naphthyl, fluorenyl and benzyl, particularly alkyl-substituted and alkoxy-substituted phenyl and benzyl. Particularly preferred R and R^1 groups include straight and branched chain C_{1-8}-alkyl substituted phenyl and benzyl such as tert-butylphenyl, tert-butylbenzyl, sec-butylphenyl, sec-butylbenzyl, n-butylphenyl, n-butylbenzyl, iso-butylphenyl, iso-butylbenzyl, pentylphenyl, pentylbenzyl, hexylphenyl, hexylbenzyl and the like; straight and branched chain C_{1-8}-alkoxy (including haloalkoxy, i.e. alkoxy substituted by F, Cl, Br and/or I) substituted phenyl and benzyl such as butoxyphenyl, butoxybenzyl, pentoxyphenyl, pentoxybenzyl, hexoxyphenyl, hexoxybenzyl, trifluoromethoxyphenyl, trifluorobenzyl, fluoro and the like; alkaryl (including alkoxyaryl) substituted phenyl and benzyl, particularly substituted and unsubstituted benzyl and benzyloxy (especially -$OCH_2C_6H_5$). Cycloalkyl and aryl (particularly carbocyclic aryl) such as substituted phenyl, benzyl and naphthyl are also preferred R and R^1 groups such as biphenyl, phenylbenzyl (i.e. -$CH_2C_6H_4C_6H_5$), cyclohexylphenyl, cyclohexylbenzyl and the like. Halo (i.e., F, Cl, Br and/or I) substituted R and R^1 groups are also preferred including halo-substituted phenyl, naphthyl and benzyl. Specifically preferred compounds of Formula XIII above include N-(4-sec-butylphenyl)-N-benzylguanidine; N-(5-acenaphthyl)-N-benzylguanidine; N-(3-acenaphthyl)-N-benzylguanidine; N-(5-acenaphthyl)-N-(4-isopropylbenzyl)guanidine; N-(3-acenaphthyl)-N-(4-isopropylbenzyl)guanidine; N-(4-cyclohexylphenyl)-N-(4-isopropylbenzyl)guanidine; N-(4-cyclohexylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(2-fluorenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-sec-butylphenyl)-N-(cinnamylmethylene)guanidine; N-(4-n-butoxyphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-biphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(5-indanyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-trifluoromethoxyphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(5-acenaphthyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-acenaphthyl)-N-(4-tert-butylbenzyl)guanidine;

N-(methoxy-1-naphthyl)-N-(4-tert-butylbenzyl)guanidine; N-(1-naphthyl)-N-(4-tert-butylbenzyl) guanidine; N-(3-iodophenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-chloro-1-naphthyl)-N-(4-tert-benzyl)guanidine; N-(4-tert-butylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-iodophenyl)-N-(4-tert-butylbenzyl)guanidine; N-(1-naphthylmethyl)-N-(4-tert-butylbenzyl)guanidine; N-(5-acenaphthyl)-N-(3-phenoxybenzyl)guanidine; N-(3-trifluoromethylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-methylthiophenyl)-N-(4-tert-butylbenzyl)guanidine; N-(5-acenaphthyl)-N-(3-2-iodobenzyl)guanidine; N-(5-acenaphthyl)-N-(cinnamyl)guanidine; N-(5-acenaphthyl)-N-(4-iodobenzyl)guanidine; N-(5-acenaphthyl)-N-(4-trifluoromethoxybenzyl)guanidine; and pharmaceutically acceptable salts thereof. Such compounds are disclosed in International Application PCT/US95/01536, incorporated herein by reference.

A still further group of preferred compounds for use in the present methods are guanidines having a substituent of substituted or unsubstituted fluorenyl, phenanthracenyl, anthracenyl and fluoranthenyl, including compounds of the Formulae I, II or III above and having at least one guanidine substituent of substituted or unsubstituted fluorenyl, substituted or unsubstituted phenanthracenyl, substituted or unsubstituted anthracenyl and substituted or unsubstituted fluoranthenyl. Specifically preferred compounds include N,N'-bis(2-fluorenyl)guanidine; N,N'-bis(2-fluorenyl)-N-methylguanidine; N,N'-bis(2-fluorenyl)-N,N'-dimethylguanidine; N,N'-bis(anthracenyl)guanidine; N,N'-bis(anthracenyl)-N-methylguanidine; N,N'-bis(anthracenyl)-N,N'-dimethylguanidine; N,N'-bis(phenanthracenyl)guanidine; N,N'-bis(phenanthracenyl)-N-methylguanidine; N,N'-bis(phenanthracenyl)-N,N'-dimethylguanidine; N,N'-bis(fluoranthenyl)guanidine; N,N'-bis(fluoroanthenyl)-N-methylguanidine; N,N'-bis(fluoroanthenyl)-N,N'-dimethylguanidine; N-(anthracenyl)-N'-(1-adamantyl)guanidine; N-(anthracenyl)-N'-(1-adamantyl)-N-methylguanidine; N-(anthracenyl)-N'-(1-adamantyl)-N'-methylguanidine; N-(anthracenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine; N-(anthracenyl)-N'-(2-adamantyl)guanidine; N-(anthracenyl)-N'-(2-adamantyl)-N-methylguanidine;

N-(anthracenyl)-N'-(2-adamantyl)-N'-methylguanidine; N-(anthracenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine; N-(phenanthracenyl)-N'-(1-adamantyl)guanidine; N-(phenanthracenyl)-N'-(1-adamantyl)-N-methylguanidine; N-(phenanthracenyl)-N'-(1-adamantyl)-N'-methylguanidine; N-(phenanthracenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine; N-(phenanthracenyl)-N'-(2-adamantyl)guanidine; N-(phenanthracenyl)-N'-(2-adamantyl)-N-methylguanidine; N-(phenanthracenyl)-N'-(2-adamantyl)-N'-methylguanidine; N-(phenanthracenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine; N-(fluorenyl)-N'-(1-adamantyl)guanidine; N-(fluorenyl)-N'-(1-adamantyl)-N-methylguanidine; N-(fluorenyl)-N'-(1-adamantyl)-N'-methylguanidine; N-(fluorenyl)-N'-(1-adamantyl)-N,N'-dimethylguanidine; N-(fluorenyl)-N'-(2-adamantyl)guanidine; N-(fluorenyl)-N'-(2-adamantyl)-N-methylguanidine; N-(fluorenyl)-N'-(2-adamantyl)-N'-methylguanidine; N-(fluorenyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine; N-(fluorenyl)-N'-(methoxynaphthyl)guanidine; N-(fluorenyl)-N'-(methoxynaphthyl)-N-methylguanidine; N-(fluorenyl)-N'-(methoxynaphthyl)-N'-methylguanidine; N-(fluorenyl)-N'-(methoxynaphthyl)-N,N'-dimethylguanidine; and pharmaceutically acceptable salts thereof. Such compounds are disclosed in International Application PCT/US95/01536, incorporated herein by reference.

Further preferred compounds for use as compound 2) in accordance with the invention include compounds of the following Formula XIV:



XIV

wherein R and R^1 are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon

atoms, substituted or unsubstituted aryloxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aralkoxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R^2 and R^3 are each independently hydrogen or a group as defined for R and R^1 above, and preferably are each substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, aminoalkyl, alkylthio or alkylsulfinyl; or R^1 and R^3 together form a ring having 5 or more ring members;

n and n' independently are each equal to 1, 2, or 3;

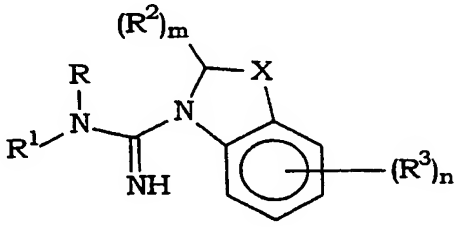
X and X' are each independently a chemical bond (i.e., a bond between the guanidine nitrogen and R or R^1), substituted or unsubstituted alkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted alkenylene having from 2 to about 8 carbon atoms, or substituted or unsubstituted alkynylene having from 2 to about 8 carbon atoms, substituted or unsubstituted heteroalkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted heteroalkenylene having 2 to about 8 carbon atoms, and substituted or unsubstituted heteroalkynylene having from 2 to about 8 carbon atoms, with at least one X and X' being other than a bond; and pharmaceutically acceptable salts thereof. Preferred compounds of Formula XIV include those where X is substituted or unsubstituted alkylene or alkenylene having 1 to about 3 carbon atoms. Specifically preferred compounds of Formula XIV include N-5-acenaphthyl-N'-benzhydrylguanidine; N-5-acenaphthyl-N'-benzhydryl-N-methylguanidne; N-5-acenaphthyl-N'-benzhydryl-N'-methylguanidine; N-5-acenaphthyl-N'-benzhydryl-N,N'-dimethylguanidine; N-3-acenaphthyl-N'-benzhydrylguanidine; N-3-acenaphthyl-N'-benzhydryl-N-methylguanidine; N-3-acenaphthyl-N'-benzhydryl-N'-methylguanidine; N-3-acenaphthyl-N'-

benzhydryl-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]guanidine; N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N-methylguanidine; N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N'-methylguanidine; N-(5-acenaphthyl)-N'-[(1-naphthyl)-methyl]-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)guanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-phenoxyethyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)guanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(1-methyl-2-(4-chlorophenyl)ethyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)guanidine; N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(1,2-diphenylethyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-(3-phenylpropyl)guanidine; N-(5-acenaphthyl)-N'-(3-phenylpropyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(2-methyl-2-phenylethyl)-N'-methylguanidine; N,N'-(sec-butylphenyl)-N'-(2-phenoxyethyl)guanidine; N,N'-(sec-butylphenyl)-N'-(2-phenoxyethyl)-N-methylguanidine; N,N'-(sec-butylphenyl)-N'-(2-phenoxyethyl)-N'-methylguanidine; N,N'-(sec-butylphenyl)-N'-(2-phenoxyethyl)-N,N'-dimethylguanidine; N-(5-acenaphthyl)-N'-((4-tert-butylphenyl)-(4-sec-butylphenyl)-methyl)guanidine; N-(5-acenaphthyl)-N'-((4-tert-butylphenyl)-(4-sec-butylphenyl)-methyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-((4-tert-butylphenyl)-(4-sec-butylphenyl)-methyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-((4-tert-butylphenyl)-(4-sec-butylphenyl)-methyl)-N,N'-dimethylguanidine; N-(4-butoxyphenyl)-N,N'-bis(4-tert-butylbenzyl)guanidine; N-(4-butoxyphenyl)-N,N'-bis(4-tert-butylbenzyl)-N-methylguanidine; N-(4-butoxyphenyl)-N,N'-bis(4-tert-butylbenzyl)-N'-methylguanidine; N-(4-butoxyphenyl)-N,N'-bis(4-tert-butylbenzyl)-N,N'-dimethylguanidine; and pharmaceutically acceptable salts of said compounds. Such compounds are disclosed in International Application PCT/US95/01536, incorporated herein by reference.

Further preferred compounds for use as compound 2) in accordance with the invention are substituted guanidines (including compounds of Formulae I, II and III above) that have a phenyl substituent that is ring substituted by one or more branched groups such as branched alkyl e.g. sec-butyl or tert-butyl, and/or one or more substituted or unsubstituted aralkoxy substituents, particularly substituted or unsubstituted benzyloxy. Preferably the phenyl substituent is ring substituted by such branched or aryloxy groups at 1, 2 or 3 ring positions. Para-substitution and meta-substitution of the phenyl substituent is preferred. Specifically preferred compounds include N,N'-di-(4-sec-butylphenyl)guanidine; N,N'-di-(4-sec-butylphenyl)-N-methylguanidine; N,N'-di-(4-sec-butylphenyl)-N,N'-dimethylguanidine; N-(2-naphthyl)-N'-(4-isopropylphenyl)guanidine; N-(2-naphthyl)-N'-(4-isopropylphenyl)-N-methylguanidine; N-(2-naphthyl)-N'-(4-isopropylphenyl)-N'-methylguanidine; N-(2-naphthyl)-N'-(4-isopropylphenyl)-N,N'-dimethylguanidine; N,N'-bis(4-tert-butylphenyl)guanidine; N,N'-bis(4-tert-butylphenyl)-N-methylguanidine; N,N'-bis(4-tert-butylphenyl)-N'-methylguanidine; N,N'-bis(4-tert-butylphenyl)-N,N'-dimethylguanidine; N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)guanidine; N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine; N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine; N-(4-sec-butylphenyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine; N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)guanidine; N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N-methylguanidine; N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N'-methylguanidine; N-(4-methoxy-1-naphthyl)-N'-(2,3,4-trichlorophenyl)-N,N'-dimethylguanidine; N,N'-bis-(4-sec-butylphenyl)-2-iminopyrimidazolidine; N,N'-bis(3-biphenyl)guanidine; N,N'-bis(3-biphenyl)-N-methylguanidine; N,N'-bis(3-biphenyl)-N'-methylguanidine; N,N'-bis(3-biphenyl)-N,N'-dimethylguanidine; N,N'-di-(3-tert-butylphenyl)guanidine; N,N'-di-(3-tert-butylphenyl)-N-methylguanidine; N,N'-di-(3-tert-butylphenyl)-N'-methylguanidine; N,N'-di-(3-tert-butylphenyl)-N,N'-dimethylguanidine; N,N'-bis-(4-methoxy-1-naphthyl)guanidine; N,N'-bis-(4-methoxy-1-naphthyl)-N-methylguanidine; N,N'-bis-(4-methoxy-1-naphthyl)-N'-methylguanidine; N,N'-bis-(4-methoxy-1-naphthyl)-N,N'-dimethylguanidine; N,N'-bis- (3-sec-butylphenyl)guanidine; N,N'-bis-(3-sec-butylphenyl)-N-

methylguanidine; N,N'-bis-(3-sec-butylphenyl)-N'-methylguanidine; N,N'-bis-(3-sec-butylphenyl)-N,N'-methylguanidine; N,N'-bis(4-n-butylphenyl)guanidine; N,N'-bis(4-n-butylphenyl)-N-methylguanidine; N,N'-bis(4-n-butylphenyl)-N'-methylguanidine; N,N'-bis(4-n-butylphenyl)-N,N'-dimethylguanidine; N,N'-(sec-butylphenyl)- N'-(n-pentyl)guanidine; N,N'-bis(3-benzyloxyphenyl)guanidine; N,N'-bis(3-benzyloxyphenyl)-N-methylguanidine; N,N'-bis(3-benzyloxyphenyl)-N,N'-dimethylguanidine; N,N'-bis(4-benzyloxyphenyl)guanidine; N,N'-bis(4-benzyloxyphenyl)-N-methylguanidine; N,N'-bis(4-benzyloxyphenyl)-N,N'-dimethylguanidine; N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)guanidine; N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N-methylguanidine; N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-methylguanidine; N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N,N'-dimethylguanidine; and pharmaceutically acceptable salts of said compounds. Such compounds are disclosed in International Application PCT/US95/01536, incorporated herein by reference.

Further preferred for use in combination with an aminoglycoside antibiotic in accordance with the invention are substituted indolinyl and indolinyl derivative compounds of the following Formula XV:



XV

wherein R and R^1 are each independently hydrogen; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl

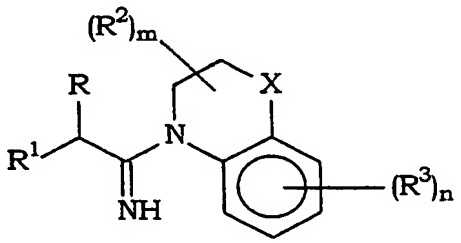
having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms, with at least one of R and R^1 being other than hydrogen;

each R^2 and each R^3 (i.e. substituent of the 4, 5, 6 and 7 aromatic ring positions) are each independently hydrogen, halogen, hydroxyl, azido, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms, or substituted or unsubstituted aralkyl having at least about 6 ring carbon atoms;

X is substituted or unsubstituted methylene ($-CH_2-$), -S- (i.e. 3-benzothiazolinylcarboximidamide compounds), -O- or substituted or unsubstituted -N-, and preferably is substituted or unsubstituted methylene;

m is 0, 1 or 2; n is 0, 1, 2, 3 or 4; and pharmaceutically acceptable salts thereof.

Also preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XVI:



XVI

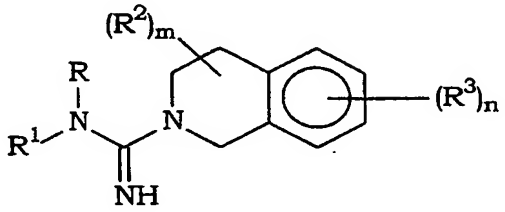
wherein R and R^1 are each independently hydrogen; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

each R^2 (i.e. substituent of the 2 and 3 ring positions) and each R^3 (i.e. substituent of the 5, 6, 7 and 8 aromatic ring positions) are each independently hydrogen, halogen, hydroxyl, azido, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms, or substituted or unsubstituted aralkyl having at least about 6 ring carbon atoms;

X is -O- (i.e. 2,3-benzmorpholinyl compounds), -S- (i.e. 2,3-benzthiomorpholinyl compounds), substituted or unsubstituted -N-, or substituted or unsubstituted methylene ($-CH_2-$);

m and n are each independently 0 (i.e. the available ring are each hydrogen-substituted), 1, 2, 3 or 4; and pharmaceutically acceptable salts thereof.

Further preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XVII:



XVII

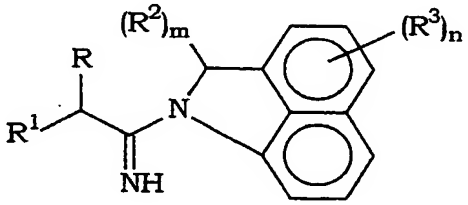
wherein R and R^1 are each independently hydrogen; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

each R^2 (i.e. substituent of the 1, 3 and 4 tetrahydroisoquinolinyl ring positions) and each R^3 (i.e. substituent of the 5, 6, 7 and 8 tetrahydroisoquinolinyl ring positions) are each independently hydrogen, halogen, hydroxyl, azido; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms,

substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms, or substituted or unsubstituted aralkyl having at least about 6 ring carbon atoms;

m is 0 (i.e. the 1, 3 and 4 tetrahydroisoquinolinyl ring positions are each hydrogen-substituted), 1, 2, 3, 4, 5 or 6; n is 0 (i.e. the 5, 6, 7 and 8 tetrahydroisoquinolinyl ring positions are each hydrogen-substituted), 1, 2, 3 or 4; and pharmaceutically acceptable salts thereof.

Further preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XVIII:



XVIII

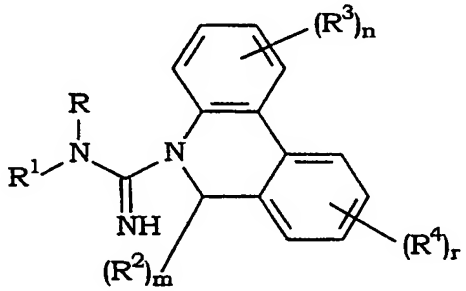
wherein R and R^1 are each independently hydrogen; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms, with at least one of R and R^1 being other than hydrogen;

each R^2 and each R^3 (i.e. substituent of the aromatic positions 3-8) are each independently hydrogen, halogen, hydroxyl, azido, substituted or

unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms, or substituted or unsubstituted aralkyl having at least about 6 ring carbon atoms;

m is 0 (i.e. the 2-benz[cd]indolinyl position is hydrogen-substituted), 1 or 2; and n is 0 (i.e. the available ring are each hydrogen-substituted), 1, 2, 3, 4, 5 or 6; and pharmaceutically acceptable salts thereof.

Also preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XIX:



XIX

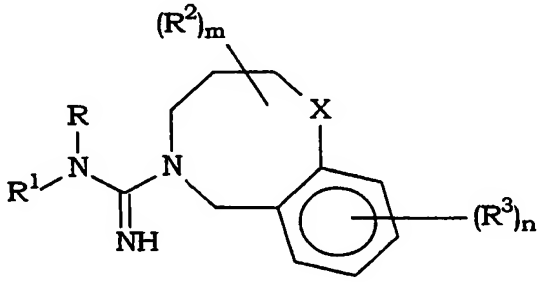
wherein R and R^1 are each independently hydrogen; substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl

having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms, with at least one of R and R^1 being other than hydrogen;

each R^2, each R^3 (i.e. substituent of the aromatic positions 1-4) and each R^4 (i.e. substituent of the aromatic positions 7-10) are each independently hydrogen, halogen, hydroxyl, azido, substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms, or substituted or unsubstituted aralkyl having at least about 6 ring carbon atoms;

m is 0 (i.e. the 5,6-dihydrophenanthridinyl ring position is hydrogen-substituted), 1 or 2; and n and r are each independently 0 (i.e. the ring positions are each hydrogen-substituted), 1, 2, 3 or 4; and pharmaceutically acceptable salts thereof.

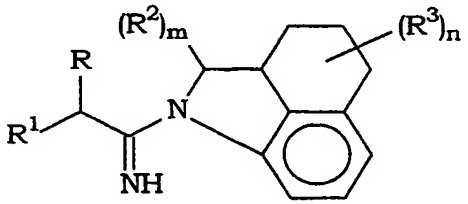
Also preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XX:



XX

wherein R, R^1, X, R^2, R^3 and n are the same as defined above for Formula XVI, but where X can also be sulfinyl (i.e.-S(O)-) or sulfonyl (i.e. -$S(O_2)$-), and m of Formula XX is an integer equal to 0-6, and preferably m is 0, 1 or 2; and pharmaceutically acceptable salts thereof. Preferred substituents of Formula XVI also will be preferred substituents at corresponding positions of compounds of Formula XX.

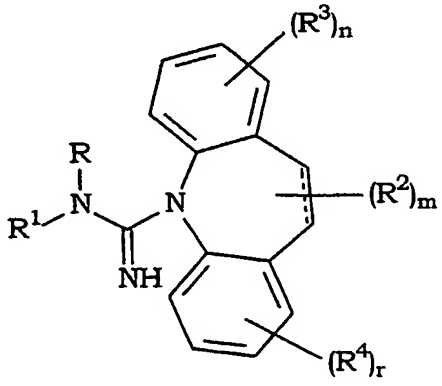
Further preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XXI:



XXI

wherein R, R^1, R^2, R^3 and m are the same as defined above for Formula XVIII, and n of Formula XXI is an integer equal to 0-9, and preferably n is 0, 1 or 2; and pharmaceutically acceptable salts thereof. It is understood that an R^3 substituent can be the same or different and may be present on either the non-aromatic or aromatic fused ring. Preferred substituents of Formula XVIII also will be preferred substituents at corresponding positions of compounds of Formula XXI.

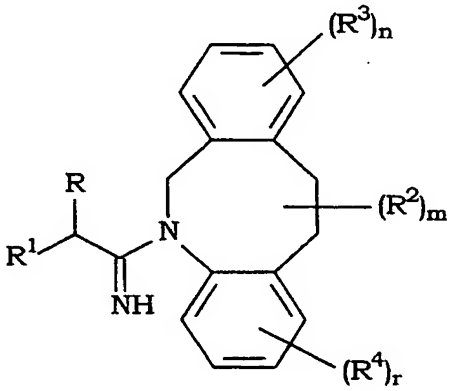
Further preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XXII:



XXII

wherein R, R^1, R^2, R^3, n and r are the same as defined above for Formula XIX, except R and R^1 each may be hydrogen, although preferably at least one of R and R^1 will be other than hydrogen, and m of Formula XXII is an integer equal to 0-4, and preferably m is 0, 1 or 2, and the dotted line in Formula XXII represents an optional carbon-carbon double bond (endocyclic bond); and pharmaceutically acceptable salts thereof. Preferred substituents of Formula XIX also will be preferred substituents at corresponding positions of compounds of Formula XXII.

Also preferred for use in combination with an aminoglycoside antibiotic in accordance with the present invention are compounds of the following Formula XXIII:



XXIII

wherein R^2, R^3, n and r are the same as defined above for Formula XIX; R and R^1 are also the same as defined above for Formula XIX, except R and R^1 each may be hydrogen, although preferably at least one of R and R^1 will be other than hydrogen; m of Formula IX is an integer equal to 0-6 (i.e. R^2 may be a substituent at any of the available three saturated ring positions), and preferably m is 0, 1 or 2.

For each of Formulae XV through XXIII preferably at least one of R and R^1 is a carbocyclic aryl, aralkyl, or heteroaromatic or heteroalicyclic group, particularly substituted or unsubstituted phenyl or naphthyl. More preferably, for each of Formulae XV through XXIII, R is a carbocyclic aryl, heteroaromatic or heteroalicyclic group, and R^1 is a non-aryl group, particularly hydrogen or substituted or unsubstituted alkyl, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, or aminoalkyl. Substituted or

unsubstituted phenyl or naphthyl are preferred R groups of Formulae XV through XXIII. Generally more preferred R^1 groups are hydrogen and substituted or unsubstituted alkyl such as substituted or unsubstituted alkyl having 1 to about 6 carbon atoms or 1 to about 3 carbon atoms.

Specifically preferred compounds of Formula XV include the following:

N-(4-benzyloxyphenyl)-1-indolinylcarboximidamide;
N-(4-methoxynaphthyl)-1-indolinylcarboximidamide;
N-(1-naphthyl)-1-indolinylcarboximidamide;
N-(3,4-dimethoxynaphthyl)-1-indolinylcarboximidamide;
N-(3,4-dichlorophenyl)-1-indolinylcarboximidamide;
N-(1-naphthyl)-1-(7-ethyl)-indolinylcarboximidamide;
N-(2-naphthyl)-1-(7-ethyl)-indolinylcarboximidamide;
N-(4-sec-butylphenyl)-1-indolinylcarboximidamide;
N-(2,3-dichlorophenyl)-1-indolinylcarboximidamide;
N-(2,3-dimethylphenyl)-1-indolinylcarboximidamide;
N-(5,6,7,8-tetrahydro-1-naphthyl)-1-indolinylcarboximidamide;
N-(2-biphenyl)-1-indolinylcarboximidamide;
N-(1-naphthyl)-N-methyl-1-indolinylcarboximidamide;
N-(2-naphthyl)-1-indolinylcarboximidamide;
N-phenyl-1-indolinylcarboximidamide;
N-(2-chlorophenyl)-1-indolinylcarboximidamide;
N-(2-methylphenyl)-1-indolinylcarboximidamide;
N-(3-methylphenyl)-1-indolinylcarboximidamide;
N-(2,5-dimethylphenyl)-1-indolinylcarboximidamide;
N-(2,5-dibromophenyl)-1-indolinylcarboximidamide;
N-(2,5-dichlorophenyl)-1-indolinylcarboximidamide;
N-(5-acenaphthyl)-1-(5-methoxy)-indolinylcarboximidamide;
N-(5-acenaphthyl)-1-(5-bromo)-indolinylcarboximidamide;
N-(2,3-dimethoxyphenyl)-1-indolinylcarboximidamide;
N-methyl-N-(4-sec-butylphenyl)-1-indolinyl-carboximidamide;
N-(2-tolyl)-1-(3-benzothiazolinyl)-carboximidamide;
N-5-indanyl-1-indolinyl-carboximidamide;
N-(3,4-dimethylphenyl)-1-indolinyl-carboximidamide;

N-(2,3,4-trichlorophenyl)-1-indolinyl-carboximidamide;
N-(2-naphthyl)-1-indolinyl-carboximidamide;
N-(3-biphenyl)-1-indolinyl-carboximidamide;
N-(8-quinolinyl)-1-indolinyl-carboximidamide;
N-(2-tolyl)-1-(4-methoxylindolinyl)-carboximidamide;
N-(2-tolyl)-1-(3-methylindolinyl)-carboximidamide;
N-(2,4-dichlorophenyl)-1-indolinyl-carboximidamide;
N-(2-methoxylphenyl)-1-indolinyl-carboximidamide;
N-(2-trifluoromethyl)-1-indolinyl-carboximidamide;
N-(4-methoxynaphthyl)-1-(4-methoxyindolinyl)-carboximidamide;
N-(4-methoxynaphthyl)-1-(4-chloroindolinyl)-carboximidamide;
N-(2,4-dimethoxyphenyl)-1-indolinyl-carboximidamide;
N-(2,4-dimethylphenyl)-1-indolinyl-carboximidamide;
N-(2,4-difluorophenyl)-1-indolinyl-carboximidamide;
N-(4-methoxy-2-nitrophenyl)-1-indolinyl-carboximidamide;
N-(4-methoxyphenyl)-1-indolinyl-carboximidamide;
N-(2,5-dichlorophenyl)-1-indolinyl-carboximidamide;
N-(4-chlorophenyl)-1-indolinyl-carboximidamide;
N-(1-naphthyl)-1-(5-fluoroindolinyl)-carboximidamide;
N-(4,5-dimethylnaphthyl)-1-indolinyl-carboximidamide;
N-(5-acenaphthyl)-1-(4-methoxyindolinyl)-carboximidamide;
N-6-(benz[cd]indol-2(1H)-one)-1-indolinyl-carboximidamide;
N-(2,3-difluorophenyl)-1-indolinyl-carboximidamide;
N-(2-(4'-methoxy)biphenyl)-1-indolinyl-carboximidamide;
N-(2-tert-butylphenyl)-1-indolinyl-carboximidamide;
N-(3,5-dichlorophenyl)-1-indolinyl-carboximidamide;
N-(2-pyrrolylphenyl)-1-indolinyl-carboximidamide;
N-(4-fluorenyl)-1-indolinyl-carboximidamide;
N-(6-coumarinyl)-1-indolinyl-carboximidamide;
N-(3-isopropylphenyl)-1-indolinyl-carboximidamide;
N-(5-methoxynaphthyl)-1-indolinyl-carboximidamide;
N-(3-(1H-imidazol-1-yl)-1-indolinyl-carboximidamide;
N-(3-quinolinyl)-1-indolinyl-carboximidamide;
N-(6-indazole)-1-indolinyl-carboximidamide;

N-(2-piperidinylphenyl)-1-indolinyl-carboximidamide;
N-(2-methylmercapto)phenyl-1-indolinyl-carboximidamide;
N-(1-methylsulfoxyphenyl)-1-indolinyl-carboximidamide;
N-(2-naphthyl)-1-(5-fluoroindolinyl)-carboximidamide; and pharmaceutically acceptable salts of those compounds.

N-(1-naphthyl)-1-indolinylcarboximidamide and pharmaceutically acceptable salts thereof are particularly preferred compounds of Formula XV.

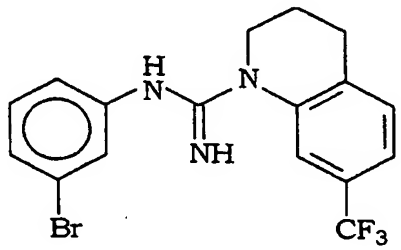
Specifically preferred compounds of Formula XVI include the following:
N-(1-naphthyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(7-methyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(2-trifluoromethyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(4-benzyloxyphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(4-methoxynaphthyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3,4-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-methoxy)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-bromo)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(7-ethyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(4-sec-butylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-dimethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(5,6,7,8-tetrahydro-1-naphthyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-biphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3-biphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;

N-(2-ethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3-ethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dimethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-ethylphenyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3-methylthiophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-difluorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(1-naphthyl)-1-(6-methyl-1,2,3,4-tetrahydroquinoline)carboximidamide;
N-(1-naphthyl)-4-(2,3-dihydro[1,4]benzothiazinyl)carboximidamide;
N-(1-naphthyl)-4-(2,3-dihydro[1,4]benzoxazinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-[7-[trifluoromethyl)-1,2,3,4-tetrahydroquinoline]carboximidamide;
N-(1-naphthyl)-1-(2-methyl-1,2,3,4-tetrahydroquinolin-1-yl)carboximidamide;
N-(3-methylthiophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-difluorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-[2-chloro-5-(trifluoromethyl)phenyl]-1-(7-(trifluoromethyl)-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-fluorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3,4-difluorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,4,5-trichlorophenyl)-1-(7-(trifluoromethyl)-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3,4-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-trifluoromethoxyphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-4-(2,3-dihydro-6-trifluoromethyl-[1,4]-benzothiazinyl)carboximidamide;
N-(2,5-dibromophenyl)-4-(2,3-dihydro-4-oxo-6-trifluoromethyl-[1,4]-benzothiazinyl)-carboximidamide;

N-(2-chloro-5-thiomethylphenyl)-1-(7-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-methylthiophenyl)-1-(6-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-sulfinylmethylphenyl)-1-(6-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-sulfonylmethylphenyl)-1-(6-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-[6-(trifluoromethyl)-1,2,3,4-tetrahydroquinolinyl]carboximidamide;
N-(2,5-dimethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(3,5-dichlorophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-thiomethylphenyl)-1-(1,2,3,4-tetrahydroquinoline)carboximidamide;
N-(2-methylthiophenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-ethoxyphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-fluoro-5-trifluoromethylphenyl)-4-(6-chloro-[1,4]-benzothiazinyl)-carboximidamide;
N-(2-biphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-4-(2,3-dihydro-1-dioxo-6-trifluoromethyl)-([1,4]-bezothiazinyl)carboximidamide;
N-(2-ethylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(8-quinolinyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-methylsulfonylphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,5-dibromophenyl)-4-(6-chloro-[1,4]-benzothiazinyl)carboximidamide;
N-phenyl-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-chloro-5-methylthiophenyl)-1-(7-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)-carboximidamide;
N-(3-trifluoromethoxyphenyl)-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;

N-(2-trifluoromethoxyphenyl)-N-methyl-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2,3-difluorophenyl)-N-methyl-1-(1,2,3,4-tetrahydroquinolinyl)carboximidamide;
N-(2-trifluoromethoxyphenyl)-1-(6-trifluoromethyl-1,2,3,4-tetrahydroquinolinyl)-carboximidamide;
N-(1-naphthyl)-4-(6-chloro-2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(5-acenaphthyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(2,3-difluorophenyl)-N-methyl-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(1-naphthyl)-4-(6-trifluoromethyl-2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(5,6,7,8-tetrahydro-1-naphthyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(3-biphenyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(2-naphthyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(3,5-dichlorophenyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(2,3-difluorophenyl)-4-(2,3-dihydro-[1,4]-benzothiazinyl)carboximidamide;
N-(1-naphthyl)-4-(2,3-dihydro-6-trifluoromethylbenzo[1,4]-1-oxo-thiazinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroquinolinyl) carboximidamide; and pharmaceutically acceptable salts thereof.

Particularly preferred compounds of Formula XVI include the following structure and pharmaceutically acceptable salts thereof:



Specifically preferred compounds of Formula XVII include the following:

N-(1-naphthyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(1-naphthyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(1-naphthyl)-1-(7-methyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,5-dibromophenyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(1-naphthyl)-1-(2-trifluoromethyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(4-benzyloxyphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(4-methoxynaphthyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(3,4-dichlorophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(5-acenaphthyl)-1-(5-methoxy)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(5-acenaphthyl)-1-(5-bromo)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(1-naphthyl)-1-(7-ethyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(4-sec-butylphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,3-dichlorophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,3-dimethylphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(5,6,7,8-tetrahydro-1-naphthyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2-biphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(3-biphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(1-naphthyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2-ethylphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(3-ethylphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,5-dimethylphenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2-chloro-5-ethylphenyl)-1-(7-trifluoromethyl)-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,5-dibromophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;

N-(2,5-dichlorophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;
N-(3-methylthiophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;
N-(2,3-difluorophenyl)-1-(1,2,3,4-tetrahydroisoquinolinyl)carboximidamide;
and pharmaceutically acceptable salts of said compounds.

Specifically preferred compounds of Formula XVIII include the following:

N-(3-biphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(1-naphthyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2-methylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2,3-dimethylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2,5-dimethylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(4-benzyloxyphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(4-methoxynaphthyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(3,4-dichlorophenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-methoxy)-1-(benz[cd]indolinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-bromo)-(benz[cd]indolinyl)carboximidamide;
N-(1-naphthyl)-1-(7-ethyl)-(benz[cd]indolinyl)carboximidamide;
N-(4-sec-butylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(3-methylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(5,6,7,8-tetrahydro-1-naphthyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2-biphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(1-naphthyl)-1-(7-trifluoromethyl)-(benz[cd]indolinyl)carboximidamide;
N-(3-ethylphenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2,5-dibromophenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2,5-dichlorophenyl)-1-(benz[cd]indolinyl)carboximidamide;
N-(2-ethylphenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(2-methoxyphenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(2-biphenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(2-chlorophenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(2,4-dimethoxyphenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(2,4-dichlorophenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(4-fluoro-2-methylphenyl)-(1-benz[cd]indolinyl)carboximidamide;

N-(2,3-dichlorophenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(3-methylmercaptophenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(3-bromophenyl)-(1-benz[cd]indolinyl)carboximidamide;
N-(3-methylcarboxylphenyl)-(1-benz[cd]indolinyl)carboximidamide;
and pharmaceutically acceptable salts of said compounds.

N-(2-methylphenyl)-1-(benz[cd]indolinyl)carboximidamide and pharmaceutically acceptable salts thereof are particularly preferred compound of Formula XVIII.

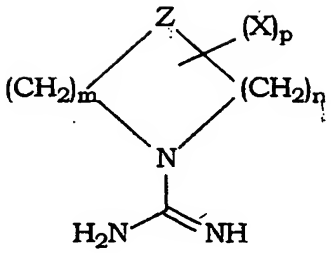
Specifically preferred compounds of Formula XIX include the following:
N-(1-naphthyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(4-benzyloxyphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(4-methoxynaphthyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(3,4-dichlorophenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-methoxy)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(5-acenaphthyl)-1-(5-bromo)-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(1-naphthyl)-1-(7-ethyl)-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(4-sec-butylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2,3-dichlorophenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2,3-dimethylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(5,6,7,8-tetrahydro-1-naphthyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2-biphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(3-biphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(1-naphthyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(1-naphthyl)-1-(7-trifluoromethyl)-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2-methylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(3-ethylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2,5-dimethylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;
N-(2-ethylphenyl)-1-(5,6-dihydrophenanthridinyl)carboximidamide;

N-(2,5-dibromophenyl)-2,3,4,5-tetrahydro-[1,5]-benzothiazepin-5-yl)carboximidamide;
N-(2,5-dibromophenyl)-(1-oxo-2,3,4,5-tetrahydro-[1,5]-benzothiazepin-5-yl]carboximidamide; and pharmaceutically acceptable salts of said compounds.

Specifically preferred compounds of Formula XXI include the following:
N-(4-methoxynaphthyl)-1-(2a,3,4,5-tetrahydrobenz[cd]indolinyl)-carboximidamide;
N-(5-acenaphthyl)-1-(2a,3,4,5-tetrahydrobenz[cd]indolinyl)-carboximidamide;
N-(4,5-dimethylnaphthyl)-1-(2a,3,4,5-tetrahydrobenz[cd]indolinyl)-carboximidamide;
N-(3,5-dichlorophenyl)-1-(2a,3,4,5-tetrahydrobenz[cd]indolinyl)-carboximidamide; and pharmaceutically acceptable salts thereof.

Specifically preferred compounds of Formulae XXII and XXIII include the following:
1-(5,6,11,12-tetrahydrodibenz[b,f]azocin)-carboximidamide;
N-(4'-sec-butylphenyl)-1-(5,6,11,12-tetrahydrodibenz[b,f]azocin)carboximidamide;
1-(dibenz[b,f]azepinyl)carboximidamide;
1-(10,11-dihydro-[5H]-dibenz[b,f]azepinyl)carboximidamide;
N-(1-naphthyl)-1-(dibenz[b,f]azepinyl)carboximidamide;
N-(4-butoxyphenyl)-1-(dibenz[b,f]azepinyl)carboximidamide; and pharmaceutically acceptable salts thereof.

Additional preferred compounds for use in combination with an aminoglycoside antibiotic include imine-substituted compounds of the following Formula XXIV:



XXIV

wherein Z is sulfur, oxygen, carbon or nitrogen;

m and n are each independently an integer from 0 to 4, and the sum of m and n is at least 2, preferably is 3, 4, 5 or 6, more preferably 3, 4 or 5;

each X is independently substituted or unsubstituted alkyl preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsilyl preferably having 1 to about 20 carbon atoms and 1 or more Si atoms; substituted or unsubstituted alkenyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy preferably having from 1 to about 20 carbon atoms, including haloalkoxy; substituted or unsubstituted alkylthio preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylamino preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl preferably having at least about 6 ring carbon atoms; substituted or unsubstituted aralkyl preferably having from 7 to about 18 carbons; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms;

p is an integer equal to 0 (where the ring is substituted only by the depicted-C(=NH)NH_2 substituent) to 14, more typically from 0 to about 4; and pharmaceutically acceptable salts thereof.

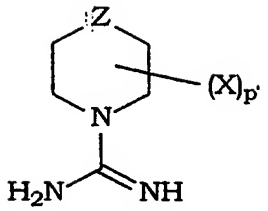
In Formula XXIV, substituted or unsubstituted methylene (-CH_2-) is a generally preferred Z ring member. Generally preferred X groups include substituted and unsubstituted alkyl, substituted and unsubstituted

alkylsilyl, substituted and unsubstituted alkenyl, substituted and unsubstituted alkynyl, substituted and unsubstituted alkylthio, substituted and unsubstituted alkylamino, substituted and unsubstituted alkylsulfinyl, substituted and unsubstituted alkylsulfonyl, substituted and unsubstituted aralkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaromatic or heteroalicyclic groups.

In Formula XXIV, particularly preferred X groups included substituted and unsubstituted alkyl and substituted and unsubstituted carbocyclic aryl, particularly substituted and unsubstituted naphthyl or phenyl such as naphthyl or phenyl substituted by alkyl or haloalkyl having 1 to about 6 carbons, halogen, alkylthio, particularly alkylthio having 1 to about 6 carbon atoms such as methylthio and ethylthio, and alkylsilyl preferably having 1 to about 15 carbon atoms.

It is understood that the imine-substituted ring nitrogen shown in the above Formula XXIV generally would not be substituted by an X group. It is further understood that the ring methylene (CH_2) groups (which include Z where Z is carbon) of the above Formula XXIV will include only a single hydrogen if the methylene unit is mono-substituted by an X group, i.e. the methylene unit will be (CHX), or the methylene unit will contain no hydrogens if di-substituted by X groups, i.e. the methylene unit will be (CXX). It is also understood the range of p values will depend in part on the sum of m and n as well as the valence of the Z ring substituent. Thus, for example, if the sum of m and n is 4 and without limitation on the Z ring member, p will be an integer of from 0 to 10, but if Z is specified to be oxygen, then p will be an integer of from 0 to 8, or if Z is nitrogen then p will be an integer of from 0 to 10.

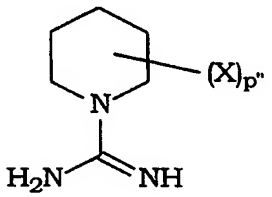
Generally preferred compounds of Formula XXIV include six-member ring compounds (i.e. where the sum of m and n above is four), particularly compounds of the following Formula XXIVa:



XXIVa

wherein for Formula XXIVa, Z and X are each the same as defined above for Formula XXIV; p' is an integer of from 0 (where the ring is substituted only by the $-C(=NH)NH_2$ substituent) to 10, more typically from 0 to about 4; and pharmaceutically acceptable salts thereof.

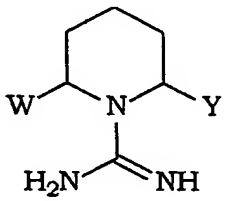
Particularly preferred compounds of Formula XXIV are substituted piperidines of the following Formula XXIVb:



XXIVb

wherein X is the same as defined above for Formula XXIV; p'' is an integer of from 0 (where the ring is substituted only by the depicted imine) to 10, more typically from 0 to about 4; and pharmaceutically acceptable salts thereof.

Preferred compounds of the invention have at least two ring substituents ($p \geq 2$ in Formula XXIV), particularly 2,6-substituted compounds of Formula XXIVa, such as the following substituted piperidine compounds of Formula XXIVc:



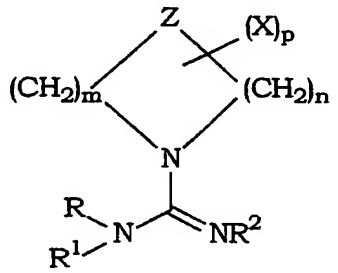
XXIVc

wherein W and Y are each independently substituted or unsubstituted alkyl preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsilyl preferably having 1 to about 20 carbon atoms and 1 or more Si atoms; substituted or unsubstituted alkenyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy preferably having from 1 to about 20 carbon atoms, including haloalkoxy; substituted or unsubstituted alkylthio preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted aminoalkyl preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl preferably having at least about 6 ring carbon atoms; substituted or unsubstituted aralkyl preferably having from 7 to about 18 carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms; and pharmaceutically acceptable salts thereof.

In Formula XXIVc, generally preferred W and Y groups include substituted and unsubstituted alkyl, substituted and unsubstituted alkylsilyl, substituted and unsubstituted alkenyl, substituted and unsubstituted alkynyl, substituted and unsubstituted alkylthio, substituted and unsubstituted alkylamino, substituted and unsubstituted alkylsulfinyl, substituted and unsubstituted alkylsulfonyl, substituted and unsubstituted aralkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaromatic or heteroalicyclic groups.

In Formula XXIVc, particularly preferred W and Y groups included substituted and unsubstituted alkyl and substituted and unsubstituted carbocyclic aryl, particularly substituted and unsubstituted naphthyl or phenyl such as naphthyl or phenyl substituted by alkyl or haloalkyl having 1 to about 6 carbons, halogen, alkylthio, particularly alkylthio having 1 to about 6 carbon atoms such as methylthio, and alkylsilyl preferably having 1 to about 15 carbon atoms.

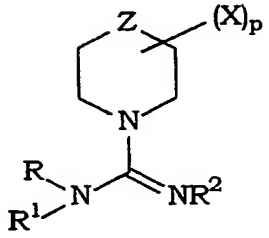
Further preferred for use in combination with an aminoglycoside antibiotic are imine-substituted compounds that are substituted by a group other than hydrogen on the imine or adjacent non-cyclic nitrogen. Preferred are compounds of the following Formula XXV:



XXV

wherein in Formula XXV, Z, X, p, m and n are the same as defined above for Formula I; R, R^1 and R^2 are each independently hydrogen; hydroxy; substituted or unsubstituted alkanoyl having from 1 to about 20 carbon atoms; substituted or unsubstituted alkanoyloxy having from 1 to about 20 carbon atoms; substituted or unsubstituted alkyl preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkenyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkynyl preferably having from 2 to about 20 carbon atoms; substituted or unsubstituted alkoxy preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylthio preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylamino preferably having from 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfinyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted alkylsulfonyl preferably having 1 to about 20 carbon atoms; substituted or unsubstituted carbocyclic aryl having at least about 6 ring carbon atoms; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 hetero atoms, with at least one of R, R^1 and R^2 being other than hydrogen; and pharmaceutically acceptable salts thereof.

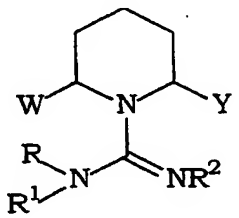
Preferred compounds of Formula XXV include six-member ring compounds (sum of m and n above is four), particularly compounds of the following Formula XXVa:



XXVa

wherein in Formula XXVa, Z and X are each the same as defined above for Formula I; p is an integer of from 0 to 10, more typically 0 to about 4; R, R^1 and R^2 are each the same as defined above for Formula XXV; and pharmaceutically acceptable salts thereof. Substituted piperidine compounds are generally preferred, i.e. where Z is carbon.

Also preferred are compounds of Formula XXV that have at least two ring substituents ($p \geq 2$ in Formula XXV), particularly 2,6-substituted compounds of Formula XXVa, such as the following piperidine compounds of Formula XXVb:



XXVb

wherein W and Y are the same as defined above for Formula XXIVc; R, R^1 and R^2 are each the same as defined above for Formula XXV; and pharmaceutically acceptable salts thereof.

Generally preferred X, W and Y groups of compounds of Formula XXV, XXVa and XXVb include substituted and unsubstituted alkyl, substituted and unsubstituted alkylsilyl, substituted and unsubstituted alkenyl, substituted and unsubstituted alkynyl, substituted and unsubstituted alkylthio, substituted and unsubstituted alkylamino,

substituted and unsubstituted alkylsulfinyl, substituted and unsubstituted alkylsulfonyl, substituted and unsubstituted aralkyl, substituted and unsubstituted carbocyclic aryl, and substituted and unsubstituted heteroaromatic or heteroalicyclic groups.

Particularly preferred X, W and Y groups of compounds of Formula XXV, XXVa and XXVb include substituted and unsubstituted alkyl and substituted and unsubstituted carbocyclic aryl, particularly substituted or unsubstituted naphthyl or phenyl such as naphthyl or phenyl substituted by alkyl or haloalkyl having 1 to about 6 carbons, halogen, alkylthio, particularly alkylthio having 1 to about 6 carbon atoms such as methylthio or ethylthio, and alkylsilyl preferably having 1 to about 15 carbon atoms.

Preferred R and R^1 groups of compounds of Formulae XXV, XXVa and XXVb include substituted and unsubstituted carbocyclic aryl and heteroaromatic and heteroalicyclic groups. Particularly preferred R and R^1 groups are substituted and unsubstituted naphthyl and phenyl groups, such as naphthyl or phenyl substituted at one or more ring positions by alkyl or haloalkyl having 1 to about 6 carbons, halogen, alkylthio, particularly alkylthio having 1 to about 6 carbon atoms such as methylthio. Other preferred R and R^1 groups include hydroxy, alkyl, alkenyl, alkynyl, alkoxy, alkylthio, alkylamino, alkylsulfinyl, alkylsulfonyl, substituted or unsubstituted alkanoyl and substituted or unsubstituted alkanoyloxy. Generally preferred are compounds of Formulae XXV, XXVa and XXVb are those where at least of one of R and R^1 is other than hydrogen, and R^2 is hydrogen.

As with compounds of Formula XXIV, it is understood with respect to the compounds of Formula XXV that the depicted imine-substituted ring nitrogen would not be substituted by an X group. It is further understood that the ring methylene groups (CH_2) of the above Formula XXV will include only a single hydrogen if the methylene unit is mono-substituted by an X group, i.e. the methylene unit will be (CHX), or the methylene unit will contain no hydrogens if di-substituted by X groups, i.e. the methylene unit will be (CXX). It is also understood the range of p values will depend in part on the sum of m and n as well as the valence of the Z ring substituent.

Specifically preferred compounds of Formulae XXIV and XXV include the following:

N-carboximidamide-r-2, c-6-di(4-methylphenyl)piperidine;

N-carboximidamide-r-2, c-6-di(4-isopropylphenyl)piperidine;

N-carboximidamide-r-2, t-6-di(4-methylphenyl)piperidine;

N-carboximidamide-r-2, c-6-diphenylpyrrolidine;

N-(N'-phenyl)carboximidamide-r-2, c-6-diphenylpiperidine;

and pharmaceutically acceptable salts thereof. See *General of Organic Chemistry*, 56:4833-4840 (1991) for discussion of the nomenclature of these preferred compounds. The structural formulae of these preferred compounds are also shown in the examples, which follow.

With respect to the above compounds 2), in addition to the above-discussed suitable and preferred substituent groups, it is further noted that suitable halogen groups of compounds for use in the present methods include F, Cl, Br and I; preferred alkyl groups include those having 1 to about 12 carbon atoms, more preferably 1 to about 10 carbon atoms such as methyl, ethyl, n-propyl, iso-propyl, n-butyl, t-butyl, iso-butyl, sec-butyl, pentyl, hexyl, heptyl, etc.; and preferred alkenyl and alkynyl groups include those groups having one or more unsaturated linkages, preferably one or two unsaturated linkages and from 2 to about 12 carbon atoms, more preferably 2 to about 8 carbon atoms. Each of the terms alkyl, alkenyl and alkynyl as used herein may refer to both cyclic and noncyclic groups, unless otherwise specified. Preferred alkoxy groups of compounds for use in the present methods include groups having one or more oxygen linkages and from 1 to about 12 carbon atoms, more preferably 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbons. Straight and branched chain butoxy, pentoxy, and hexoxy may be particularly preferred for some compounds. Methoxy, ethoxy and propoxy also may be preferred. Preferred aryloxy groups of compounds for use in the present methods have 6 to about 20 carbon atoms or from 6 to about 12 carbon atoms and include an oxygen atom. Substituted or unsubstituted phenoxy and naphthoxy are preferred aryloxy groups. Preferred aralkoxy groups of compounds for use in methods of the invention from 6 to about 20 carbon atoms and include an alkoxy group as specified above that contains one or more aryl substituents,

particularly one or more carbocyclic aryl substituents. Typically an oxygen will be the terminal group of the substituent. Substituted or unsubstituted benzyloxy (i.e., $C_6H_5CH_2O$-) are preferred aralkoxy groups. Preferred alkylthio groups of compounds for use in the present methods include groups having one or more thioether linkages and from 1 to about 12 carbon atoms, more preferably 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbons. Preferred aminoalkyl groups of compounds for use in the present methods include those groups having one or more primary, secondary and/or tertiary amine groups, and from 1 to about 12 carbon atoms, more preferably 1 to about 8 carbon atoms, still more preferably 1 to about 6 carbons. Secondary and tertiary amine groups are generally more preferred than primary amine moieties. Preferred alkylsulfinyl groups of compounds for use in the present methods have one or more sulfinyl (SO) groups, more typically one sulfinyl group, and from 1 to about 12 carbon atoms, more preferably 1 to about 6 carbons, and even more preferably 1-3 carbon atoms. Preferred alkylsulfonyl groups of compounds for use in the present methods have one or more sulfono (SO_2) groups, more typically one sulfono group, and from 1 to about 12 carbon atoms, more preferably 1 to about 6 carbons, and even more preferably 1-3 carbon atoms. Preferred alkenylene and alkynylene groups of compounds for use in the present methods have one or two carbon-carbon multiple bonds. Preferred heteroalkylene, heteroalkenylene and heteroalkynylene groups of compounds for use in the present methods contain 1 to about 3 heteroatoms consisting of N, O and/or S atoms. In general, heteroatoms of substituent groups will be N, O or S. Suitable heteroaromatic and heteroalicyclic groups of compounds for use in methods of the invention contain one or more N, O or S atoms and include, e.g., quinolinyl including 8-quinolinyl; indolinyl including 5-indolinyl, furyl, thienyl, pyrrolyl, thiazolyl, pyridyl, pyrimidinyl, pyridazinyl, oxazolyl and phthalimido groups all of which may be optionally independently substituted at one or more available positions and/or fused to a benzene ring; and substituted or unsubstituted tetrahydrofuranyl, tetrahydropyranyl, piperidinyl, piperazinyl, morpholino, pyrrolidinyl groups, pyrazinyl, coumarinyl, tetrahydroquinolinyl, tetrahydroisoquinolinyl, benzothiazolyl, benzotriazolyl,

and bezimidazolyl. Preferred carbocyclic aryl groups include those having about 6 to about 20 carbons, more preferably about 1 to 3 separate or fused rings and from 6 to about 18 carbon atoms such as phenyl, naphthyl, acenaphthyl, phenanthryl, anthracyl and fluorene groups. Suitable aralkyl groups contain 1 to 3 separate of fused rings and from 6 to about 18 carbon atoms such as benzyl and methylenenaphthyl (-CH_2-naphthyl).

Said substituted moieties or substituents of compounds for use in the present methods (e.g. groups designated as "substituted" rather than "unsubstituted" in the above formulae) may be substituted at one or more available positions by one or more suitable groups such as, e.g., halogen such as F, Cl, Br, or I; cyano; hydroxyl; nitro; azido; carboxy; carbocyclic aryl; alkyl groups including alkyl groups having from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkenyl and alkynyl groups including groups having one or more unsaturated linkages and from 2 to about 12 carbon atoms or from 2 to about 6 carbon atoms; alkoxy groups such as those groups having one or more oxygen linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkylthio groups such as those groups having one or more thioether linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 or 1 to about 6 carbon atoms; alkylsulfinyl such as those groups having one or more sulfinyl groups and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkylsulfonyl such as those groups having one or more sulfono groups and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms.

Specifically preferred substituted groups include carboxylic acyl groups, preferably having from 1 to about 12 or 1 to about 6 carbon atoms such as acetyl, propanoyl, iso-propanoyl, butanoyl, sec-butanoyl, pentanoyl and hexanoyl groups. Also preferred substituted moieties are alkaryl groups which include single and multiple ring compounds, including multiple ring compounds that contain separate and/or fused aryl groups, e.g., above-mentioned aryl groups substituted by one or more C_1-C_{10} alkyl groups such as phenylmethyl, phenylethyl, phenylpropyl, phenylbutyl, phenylpentyl and phenylhexyl groups as well as the branched chain isomers thereof such as

tert-butylphenyl, sec-butylphenyl, etc. Haloalkyl and haloalkoxy are also preferred, particularly fluoroalkyl and fluoroalkoxy such as trifluoromethyl and trifluoroalkoxy. Aroyl groups are also preferred substituted groups such as carbonyl substituted by phenyl, naphthyl, acenaphthyl, phenanthryl, and anthracyl groups and carboxylic acyl groups substituted by one or more aryl groups, e.g., diphenylacetoxy and fluorenecarboxy groups. Aralkanoyl groups are also preferred and include carbonyl substituted by the aralkyl groups described above. Aralkoxy groups are also preferred substituted groups and include alkoxy groups substituted by phenyl, naphthyl, acenaphthyl, phenanthyl, and anthracyl groups. Preferred substituted aryl groups include the above described aryl groups substituted by halo, hydroxy, alkyl, alkenyl, alkynyl, alkoxy, amino, aminoalkyl, thioalkyl and the like.

Other compounds suitable for use in combination with an aminoglycoside antibiotic in accordance with the present invention include N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinolinyl) guanidine; N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinolinyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinolinyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(1,2,3,4-tetrahydroquinolinyl)-N,N'-dimethylguanidine; N-(3-acenaphthyl)-N'-(indolinyl)guanidine; N-(3-acenaphthyl)-N'-(indolinyl)-N-methylguanidine; N-(3-acenaphthyl)-N'-(indolinyl)-N'-methylguanidine; N-(3-acenaphthyl)-N'-(indolinyl)-N,N'-methylguanidine; N-(5-acenaphthyl)-N'-(piperonyl)guanidine; N-(5-acenaphthyl)-N'-(piperonyl)-N-methylguanidine; N-(5-acenaphthyl)-N'-(piperonyl)-N'-methylguanidine; N-(5-acenaphthyl)-N'-(piperonyl)-N,N'-dimethylguanidine; N-(2-naphthyl)-N'-(2-adamantyl)guanidine; N-(2-naphthyl)-N'-(2-adamantyl)-N-methylguanidine; N-(2-naphthyl)-N'-(2-adamantyl)-N'-methylguanidine; N-(2-naphthyl)-N'-(2-adamantyl)-N,N'-dimethylguanidine; N,N'-bis-(5-indanyl)-guanidine; N,N'-bis(6-benz[cd]indolinyl-2[1H]-one)guanidine; N-(3-sec-butylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-tert-butylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(3-pentoxyphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(5-acenaphthyl)-N-(4-benzyloxybenzyl)guanidine; N-(4-sec-butylphenyl)-N-(4-benzyloxybenzyl)guanidine; N-(4-benzyloxyphenyl)-N-(4-benzyloxybenzyl)guanidine; N-(5-acenaphthyl)-N-(3-

benzyloxybenzyl)guanidine; N-(4-isopropylphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-benzyloxyphenyl)-N-(4-tert-butylbenzyl)guanidine; N-(4-hexylphenyl)-N-(4-tert-hexylbenzyl)guanidine; N-(4-sec-butylphenyl)-N-(4-t-butylbenzyl)-N'-pyrrolidinylguanidine; N-(4-sec-butylphenyl)-N-(4-t-butylbenzyl)-N'-(4-thiomorpholinyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-piperidinylguanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-morpholinyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-propylpiperidinyl)guanidine; N-(4-butoxyphenyl)-N-(4-tert-butylbenzyl)-N'-(4-piperidinyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-benzylpiperidinyl)guanidine; N-(4-benzyloxyphenyl)-N-(4-tert-butylbenzyl)-N'-(4-morpholinyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(1,2,3,4-tetrahydroisoquinolinyl)guanidine; N-(3-butoxy-4-methoxyphenyl)-N-(4-tert-butylbenzyl)-N'-(4-morpholinyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(3,5-dimethyl-4-morpholinyl)guanidine; N-(4-tert-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-sec-butylphenyl)-N'-(methyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-sec-butylphenyl)-N'-(methyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(phenyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-chlorophenyl)guanidine; N-(4-butoxylphenyl)-N-(4-tert-butylbenzyl)-N'-(phenyl)guanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(phenyl)-N'-methylguanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(3,4-dichlorophenyl)guanidine; N-(4-hexylphenyl)-N-(4-tert-hexylbenzyl)-N'-phenylguanidine; N-(4-sec-butylphenyl)-N-(4-tert-butylbenzyl)-N'-(4-benzyloxyphenyl)guanidine; N,N'-bis-(4-tert-butylphenyl)-N,N'-dimethylguanidine; N-(4-benzyloxyphenyl)-N'-(4-tert-butylphenyl)guanidine; N,N'-bis-(3-(1'-methyl-2'-phenyl)ethyl)guanidine; N-methyl-N-4-benzyloxyphenyl-N'-(4-tert-butylphenyl)guanidine; N,N'-bis-(4-hexylphenyl)guanidine; N-(3-(1-(4'-ethoxy)benzyl)phenethyl)-N'-(4-tert-butylphenyl)guanidine; N-(4-benzyloxyphenyl)-N'-methyl-N-(4-tert-butylphenyl)guanidine; N-(3-(4-tert-butylbenzyloxy)phenyl)-N'-(4-tert-butylphenyl)guanidine; N-(3-(1'-benzylbutyl)phenyl)-N'-(4-tert-butylphenyl)guanidine; N,N'-bis-(4-butylphenyl)-N-methylguanidine; N,N'-bis-(4-tert-butylphenyl)-N,N'-dimethylguanidine; N-(3-naphthaloxyphenyl)-

N'-(4-tertbutylphenyl)guanidine; N-(4-benzyloxyphenyl)-N'-(4-butylphenyl)guanidine; N,N'-bis-(4-butylphenyl)-N-butylguanidine; N-3-(benzyloxymethyl)phenyl-N'-(4-tert-butylphenyl)guanidine; N-(3,4-bis-butyloxyphenyl)-N'-(4-tert-butylphenyl)guanidine; N-(3-benzyloxy)phenyl-N'-(4-tert-butylphenyl)guanidine; N,N'-bis-(3-butoxy-4-methoxy)phenylguanidine; N-(4-benzyloxyphenyl)-N-methyl-N'-(4-butylphenyl)guanidine; N-(4-benzyloxyphenyl)-N'-methyl-N'-(4-butylphenyl)guanidine; N,N'-bis-(6-tetralinyl)guanidine; N-(6-tetralinyl)-N'-(4-tert-butylphenyl)guanidine; N-(5-acenaphthyl)-N'-(6-benzothiozolyl)guanidine; N-(5-acenaphthyl)-N'-(6-N-benzylindolinyl)guanidine; N-(5-acenaphthyl)-N'-(4-benzo-2,1,3-thiadizaole)guanidine; N-(5-acenaphthyl)-N'-[4-(6-methyl-benzothiazole)phenylguanidine; N-(5-acenaphthyl)-N'-(1-benz[cd]indolinyl)guanidine; N-(5-acenaphthyl)-N'-(6-benz[cd]indo-2[1H]-one)guanidine; N-(4-butoxyphenyl)-N'-(4-chlorophenylethyl)guanidine; N-(4-benzyloxyphenyl)-N,N'-diphenylguanidine; N-(4-benzyloxyphenyl)-N'-benzyl-N'-phenylguanidine; N-(3-benzyloxyphenyl)-N'-(4-thiobenzylphenyl)guanidine; N,N'-bis(4-(phenylthio)phenyl)guanidine; N,N'-bis(3-(phenylthio)phenyl)guanidine; N-(5-acenaphthyl)-N'-(2-phenylethyl)guanidine; N-(5-acenaphthyl)-N'-(3-butoxypropyl)guanidine; N,N'-bis(2,2-diphenylethyl)guanidine; N-(4-butoxyphenyl)-N'-(4-chlorophenylethyl)guanidine; N-(4-butoxyphenyl)-N-(4-chlorobenzhydryl)guanidine; (5-acenaphthyl)-N'-(phenethyl)-N'-benzylguanidine; N-(4-benzyloxyphenyl)-N'-(3-benzyloxyphenyl)-N'-(4-chlorobenzyl)guanidine; N,N'-bis(4-benzyloxyphenyl)-N'-methylguanidine; N-(4-benzyloxyphenyl)-N'-(3-benzyloxyphenyl)-N'-(4-chlorobenzyl)guanidine; N-(3-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-phenylguanidine; N-(4-sec-butylphenyl)-N'-(4-isopropoxyphenyl)-N'-phenylguanidine; N-(4-benzyloxyphenyl)-N'-(4-benzyloxyphenyl)-N'-phenylguanidine; N,N'-bis(3-octyloxyphenyl)guanidine; N,N'-bis(4-butoxyphenyl)guanidine; N,N'-bis(4-phenoxyphenyl)guanidine; N-(3-benzyloxyphenyl)-N'-(4-phenoxyphenyl)guanidine; N-(3-benzyloxyphenyl)-N'-(4-phenylazophenyl)guanidine; N,N'-bis(3-benzyloxyphenyl)-N'-methylguanidine; N-(4-benzyloxphenyl)-N'-(4-benzyloxyphenyl)-N'-

methylguanidine; N-(4-butoxyphenyl)-N'-(4-isopropoxyphenyl)guanidine; N-N'-bis(4-(1-hydroxybutyl)phenyl)guanidine; N-(4-butoxyphenyl)-N'-(3-methoxyphenyl)-N'-phenylguanidine; N-(4-secbutylphenyl)-N'-phenyl-N'-(4-(2-isopropoxy)phenyl)guanidine; and N-(4-n-butoxyphenyl)-N'-(2-(4-chlorophenyl)ethyl)guanidine; and pharmaceutically acceptable salts of thereof.

Compounds 2) for use in combination with an aminoglycoside antibiotic can be prepared in accordance with disclosed procedures. For preferred synthetic protocols, see the above-discussed U.S. Patent Nos. 4,906,779; 5,011,834; 5,190,976; 5,262,568; 5,403,861; and International Applications PCT/US91/03594; PCT/US92/01050; PCT/US92/03354; PCT/US94/06008; PCT/US94/13245; PCT/US94/13541; PCT/US95/01536; and PCTUS97/02678 and corresponding U.S. application and U.S. application 08/694,906, which are each again incorporated herein by reference. See also U.S. Patent No. 5,298,657 to Durant et al., incorporated herein by reference.

Thus, for example, guanidine compounds useful in methods of the invention can be readily prepared by the reaction of an amine, typically an amine salt such as an amine hydrochloride, with a preformed alkyl or aryl cyanamide (see S.R. Safer, et al., *J. Org. Chem.*, 13:924 (1948)) or the corresponding N-substituted alkyl or aryl cyanamide. This is a particularly suitable method for producing N,N'-diaryl-N'-alkyl in which the substituents are not identical. For a synthesis of asymmetrical guanidines, see G.J. Durant et al., *J. Med. Chem.*, 28:1414 (1985), and C.A. Maryanoff et al., *J. Org. Chem.*, 51:1882 (1986).

More particularly, substituted guanidines can be prepared suitably by reaction of an appropriate amine salt such as an amine hydrochloride with a slight molar excess (e.g., ca. 1.1 molar equivalent) of a substituted cyanamide in a suitable solvent such as toluene or chlorobenzene under an inert atmosphere such as argon or nitrogen. The reaction is then heated, e.g. from about 110 to 120°C for 2 to about 16 hours until reaction completion, e.g. as indicated by thin layer chromatography. The reaction solution is then cooled to room temperature, and suitably diluted with a solvent such as absolute alcohol. The solvent is then removed under

reduced pressure to provide the desired substituted guanidine. The crude product then can be purified e.g. by recrystallization and/or chromatography. The cyanamide and amine reagents with appropriate substituents are commercially available or can be readily prepared by known procedures. For example, the cyanamide starting material can be synthesized from the correspondingly substituted amine by treatment with cyanogen bromide (BrCN) in suitable solvent such as dry ethyl ether. The amine hydrochloride can be obtained by treatment of an appropriate amine with an excess of HCl. An alkylsulfinyl-substituted or alkylsulfonyl-substituted reagent that can provide correspondingly substituted guanidines as described above, can be provided by oxidation (e.g., H_2O_2) of alkylthio-substituted reagents.

Compounds of Formula XV through XXIII can be prepared by reaction of a suitable precursor compound, e.g. indolinyl (or derivative thereof) compound, 1,2,3,4-tetrahydroquinolinyl (or derivative thereof) compound, 1,2,3,4-tetrahydroisoquinolinyl compound, benz[cd]indolinyl compound, 5,6-dihydrophenanthridinyl compound, 2,3,4,5-tetrahydro-[1,5]-benzothiazepine compounds (or derivative thereof, e.g. where X is other atom), 2a,3,4,5-tetrabenz[cd]indoline compound, 5,6,11,12-tetrahydrodiben[b,f]azocine compound, etc. (depending on whether a compound of Formulae XV through XXIII respectively, is being prepared) with a preformed alkyl or aryl cyanamide (see S.R. Safer, et al., *J. Org. Chem.*, 13:924 (1948)) or the corresponding N-substituted alkyl or aryl cyanamide. Typically, a salt of the amine (e.g. an HCl salt) is reacted with the cyanamide.

More particularly, compounds Formulae XV through XXIII can be suitably prepared by reaction of an appropriate indolinyl (or derivative thereof) salt (to prepare compounds of Formula XV), 1,2,3,4-tetrahydroquinolinyl (or derivative thereof) salt (to prepare compounds of Formula XVI), 1,2,3,4-tetrahydroisoquinolinyl salt (to prepare compounds of Formula XVII), benz[cd]indolinyl salt (to prepare compounds of Formula XVIII), or 5,6-dihydrophenanthridinyl salt (to prepare compounds of Formula XIX) or other appropriate salt such as salts of above mentioned precursor compounds (to form compounds of Formulae XX-XXIII) with a

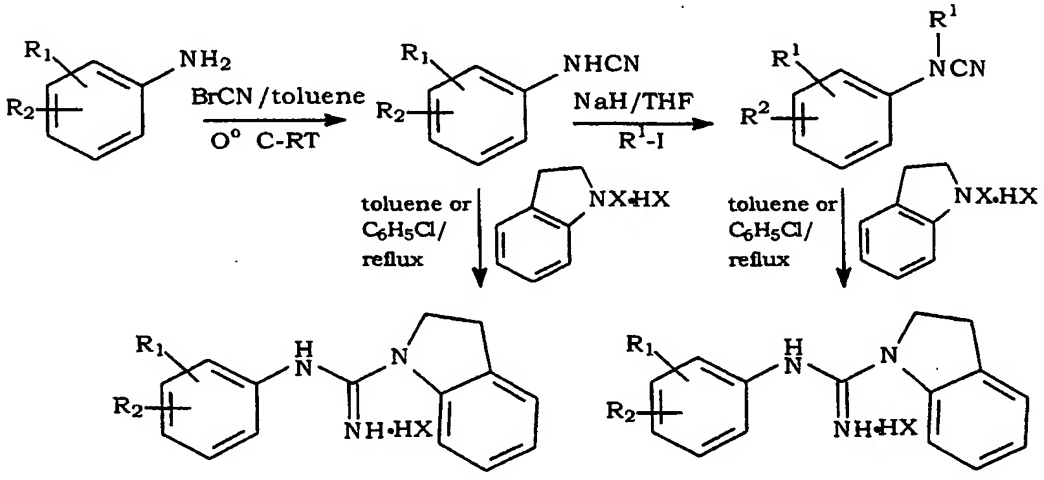
substituted cyanamide in a suitable solvent such as toluene, chlorobenzene or the like under an inert atmosphere such as argon or nitrogen as exemplified in the Scheme below. The reaction solution is then heated e.g. from about 110° to 120°C for 2 to about 16 hours until reaction completion, e.g. as indicated by thin layer chromatography. The reaction solution is then cooled to room temperature, and the solvent is then removed under reduced pressure to provide the desired compound of the invention. The crude product then can be purified by recrystallization and/or column chromatography, e.g. by elution one or more times on silica gel (e.g., 60-200 mesh, 50x w/w) with suitable solvents.

The indolinyl (or derivative thereof), 1,2,3,4-tetrahydroquinoline (or derivative thereof), 1,2,3,4-tetrahydroisoquinoline, benz[cd]indolinyl or 5,6-dihydrophenanthridinyl or other precursor such as those mentioned above (for Formulae XX-XXIII) and cyanamide reagents with appropriate substituents are commercially available or can be readily prepared by known procedures. For example, the cyanamide starting material can be synthesized from the correspondingly substituted amine by treatment with cyanogen bromide (BrCN) in a suitable solvent such as dry ethyl ether or toluene at reduced temperatures (e.g. 0°C) or room temperature. As exemplified in the Scheme below, the amine to be reacted with cyanogen bromide is substituted with the R moiety as defined above for Formulae XV through XXIII (in the Scheme, that R moiety is exemplified as phenyl which may be ring-substituted by groups R_1 and R_2). Thus, various R groups of compounds of Formula XV through XIII can be provided by use of suitable substituted amines that are reacted with BrCN, such as e.g. substituted and unsubstituted anilines as shown in the Scheme, substituted and unsubstituted 1-naphthylamine, 2-naphthylamine, acenaphthylamine, etc. R^1 groups other than hydrogen of compounds of Formulae XV through XXIII can be readily provided by reaction of a substituted cyanamide with a suitable nucleophile such as a halide reagent (e.g., a substituted or unsubstituted alkyl or alkenyl iodide or bromide). Thus, as exemplified in the Scheme below, the aryl cyanamide is reacted with NaH in a solvent of tetrahydrofuran and reacted with the iodide reagent R^1-I, such as substituted or unsubstituted methyl, ethyl, propyl, butyl, etc. iodide, an

alkenyl iodide, etc. Also, compounds of the invention having an R^1 group of methyl can be prepared by reaction of a mono-substituted amine (e.g., an aniline, naphthylamine or acenaphthylamine) with formic acid followed by treatment with lithium aluminum hydride to provide the corresponding methyl-substituted cyanamide (e.g., $C_6H_5N(CH_3)CN$ from unsubstituted aniline). Alkylsulfinyl-substituted or alkylsulfonyl-substituted reagents, that can provide correspondingly substituted compounds of the invention as described above, can be provided by oxidation (e.g., H_2O_2) of alkylthio-substituted reagents.

While the following Scheme depicts preparation of compounds of Formula XV, the same procedures can be employed to prepare compounds of Formulae XVI through XXIII by use of a 1,2,3,4-tetrahydroquinolinyl (or derivative thereof) salt, 1,2,3,4-tetrahydroisoquinolinyl salt, benz[cd]indolinyl salt or 5,6-dihydrophenanthridinyl salt or other corresponding salt for compounds of Formulae XX through XXIII, respectively, in place of the indolinyl salt shown in the Scheme.

SCHEME

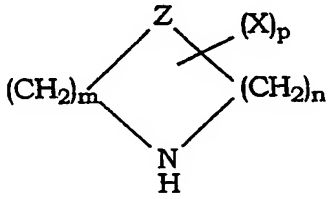


Compounds of Formula XVI where R and R^1 are each hydrogen can be prepared by reaction of 1,2,3,4-tetrahydroquinoline compound with cyanamide. R^2 substituents can be provided by reaction of a substituted or unsubstituted quinoline compound with a Grignard reagent followed by hydrogenation to provide the substituted 1,2,3,4-tetrahydroquinoline

compound. Compounds of Formulae XV, XVI and XX where X is -S(O)- or -$S(O)_2$- can be prepared by oxidation (e.g. with H_2O_2 and/or with sodium periodate) of the corresponding preformed compounds where the ring member X is -S-.

The amine starting materials are commercially available and/or can be readily prepared. For example, benz[cd]indoline and 5,6-dihydrophenanthridine reagents can be prepared treatment of a benz[cd]indo-2(1H)-one compound or 5,6-dihydrophenanthridinone compound with a base such as diborane in a suitable solvent such as tetrahydrofuran. Chiral compounds of the invention may be used as optically enriched or racemic mixtures. An optically enriched mixture contains substantially more (e.g. about 60%, 70%, 80% or 90% or more) of one enantiomer or diastereoisomer than the other stereoisomers. Optically enriched mixtures can be obtained by known procedures, e.g., column chromatography using an optically active binding material or formation of a salt using an optically active material, particularly an optically active acid. Particularly preferred optically enriched mixtures include sulfinyl-containing compound of the invention, e.g. compounds of Formulae XV, XVI or XX where X is -S(O)-, or compounds having an alkylsulfinyl or other sulfinyl substituent. Such optically active mixtures of sulfinyl-containing compounds can be readily prepared, e.g. by column chromatography using an optically active binding material.

Compounds of Formulae XXIV and XXV can be prepared by several routes. For example, compounds of Formulae XXIV and XXV can be prepared by reaction of cyanamide with a precursor derivative of Formula XXIV that does not contain the N-substituent of -$C(=NH)NH_2$ or -$C(=NR^2)NRR^1$, i.e. a compound of the following Formula XXVI (where Z, X, m, n and p are each the same as defined above for Formula XXIV):



XXIV

More particularly, compounds of Formula XXIV or XXV can be suitably prepared by reaction of a precursor compound of Formula XXVI above with cyanamide to provide compounds of Formula XXIV, or a substituted cyanamide to provide compounds of Formula XXV, in a suitable solvent such as methanol, ethanol and chloroform or the like under an inert atmosphere such as argon or nitrogen. Typically, an HCl or other acid addition salt of the precursor compound III is reacted with the cyanamide. The reaction solution is suitably heated e.g. from about 100°C or greater for 2 to about 60 hours until reaction completion, e.g. as indicated by thin layer chromatography. The reaction solution is then cooled to room temperature, and the solvent is then removed under reduced pressure to provide the desired compound of the invention. The crude product then can be purified by recrystallization and/or column chromatography, e.g. by elution one or more times on silica gel (e.g., 60-200 mesh, 50x w/w) with suitable solvents.

Precursor compounds of the above Formula XXVI may be commercially available or can be prepared by reduction of the corresponding unsaturated heterocyclic nitrogen compound, e.g. by use of a reducing agent such as sodium and ethanol. Hydrogenation also may be employed using palladium or other suitable catalyst. The nitrogen may be suitably activated during hydrogenation, e.g. with an oxycarbonyl group such as t-butoxycarbonyl or the like, which group can be then removed such as by acidic hydrolysis prior to reaction with cyanamide or other reagent.

Substituted unsaturated cyclic amine compounds to employ in such reduction reactions can be prepared by several methods. For example, an organometallic reagent can be prepared (typically Group I or II metal, particularly Li or Mg) such as by a halogen-metal exchange reaction followed by reaction of that organometallic reagent with a halopyridine or other halogen-substituted cyclic amine.

Alternatively, a substituted pyridine or other unsaturated precursor compound can be prepared by cyclization of an intermediate compound that contains the ring substituents (i.e. groups X, W and Y in the above Formulae XXIV and XXV), e.g. by cyclization of a substituted 1,5-diketopentyl compound with hydroxylamine.

Compounds of Formulae XXIV and XXV also may be prepared by reaction of a precursor compound of Formula XXVI above with cyanogen bromide to provide the N-cyano derivative (i.e. compounds of Formula XXVI above substituted at the depicted ring nitrogen by cyano). That cyano intermediate then may be suitably reacted an amine, particularly an ammonium salt such as an acetate salt, typically with heating to provide the N-imine substituted compound of Formula XXIV. Compounds of Formula XXV may be prepared by reaction of the N-cyano derivative with a primary or secondary amine (to provide the desired R and R^1 groups as defined above for Formula XXV) in the presence of a Lewis acid such as $AlCl_3$ and the like.

Alkylsulfinyl-substituted or alkylsulfonyl-substituted reagents, that can provide correspondingly substituted compounds of the invention as described above, can be provided by oxidation (e.g., H_2O_2) of alkylthio-substituted reagents.

As discussed above, methods are provided for treatment of infections, including Gram-negative and Gram-positive bacteria such as Pseudomonas aeruginosa and other Pseudomonas strains, and tuberculosis strains. In general, the therapeutic methods of the invention can be employed in therapies wherever aminoglycosides have been previously employed as well as against other infections, e.g. against infections traditionally treated with other antibacterials or antibiotics such as beta-lactams. However, in preferred aspects of the invention, the methods and compositions of the invention exhibit reduced ototoxicity relative to use of an aminoglycoside alone.

The methods of the invention in general comprise administering an aminoglycoside antibiotic in combination with a compound 2) such as a substituted guanidine or other compound as disclosed herein. The aminoglycoside and a compound 2) may be administered simultaneously, in the same or different pharmaceutical formulations, or sequentially. However, if administered sequentially, the aminoglycoside and compound 2) are preferably administered within a sufficient time to achieve the desired pharmacological effects of reduced ototoxicity.

In accordance with the invention, a combination of an aminoglycoside antibiotic and a compound 2) may be administered to a subject by a variety

of routes including oral, rectal, nasal, topical (including eye drops, buccal, sublingual), vaginal or parenteral (including subcutaneous, intramuscular and intradermal) administration.

Compounds 2) are suitably administered to a subject in the protonated and water-soluble form, e.g., as a pharmaceutically acceptable salt of an organic or inorganic acid, e.g., hydrochloride, sulfate, hemi-sulfate, phosphate, nitrate, acetate, oxalate, citrate, maleate, mesylate, etc.

It also should be appreciated that at least many of the compounds 2) may exist as any one of a number tautomeric forms. Each of such tautomeric forms is within the scope of the invention, including as defined by the above formulae. Additionally, compounds used in the methods and compositions of the invention may have asymmetric centers and occur as racemic mixtures or an optically enriched mixtures. All possible optical isomers are included in the present invention.

An aminoglycoside and compound 2) can be employed, either alone or in combination with one or more other therapeutic agents, as a pharmaceutical composition in mixture with conventional excipient, i.e., pharmaceutically acceptable organic or inorganic carrier substances suitable for a desired route of administration which do not deleteriously react with the active compounds and are not deleterious to the recipient thereof. Suitable pharmaceutically acceptable carriers include but are not limited to water, salt solutions, alcohol, vegetable oils, polyethylene glycols, gelatin, lactose, amylose, magnesium stearate, talc, silicic acid, viscous paraffin, perfume oil, fatty acid monoglycerides and diglycerides, petroethral fatty acid esters, hydroxymethyl-cellulose, polyvinylpyrrolidone, etc. The pharmaceutical preparations can be sterilized and if desired mixed with auxiliary agents, e.g., lubricants, preservatives, stabilizers, wetting agents, emulsifiers, salts for influencing osmotic pressure, buffers, colorings, flavorings and/or aromatic substances and the like which do not deleteriously react with the active compounds.

For parenteral application, particularly suitable are solutions, preferably oily or aqueous solutions as well as suspensions, emulsions, or implants, including suppositories. Ampules are convenient unit dosages.

For enteral application, particularly suitable are tablets, dragees or capsules having talc and/or carbohydrate carrier binder or the like, the carrier preferably being lactose and/or corn starch and/or potato starch. A syrup, elixir or the like can be used wherein a sweetened vehicle is employed. Sustained release compositions can be formulated including those wherein the active component is protected with differentially degradable coatings, e.g., by microencapsulation, multiple coatings, etc.

It will be appreciated that the actual preferred amounts of the components of the combination of the invention used in a given therapy will vary according to the specific compound being utilized, the particular compositions formulated, the mode of application, the particular site of administration, the age, weight, etc. of the patient, etc. Optimal administration rates for a given protocol of administration can be readily ascertained by those skilled in the art using conventional dosage determination tests conducted with regard to the foregoing guidelines. In general, a suitable effective dose of a active agents of a formulation of the invention, particularly when using more potent compounds, will be in a range of from 0.01 to 100 milligrams per kilogram of bodyweight of recipient per day of each of an aminoglycoside antibiotic and a compound 2), more typically in the range of from 0.01 to 50 milligrams per kilogram bodyweight of recipient per day of each of an aminoglycoside antibiotic and a compound 2). The desired dose is suitably administered once daily, or several sub-doses, e.g. 2 to 4 sub-doses, are administered at appropriate intervals through the day, or other appropriate schedule.

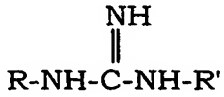
The entire text of all documents cited herein are incorporated by reference herein.

This invention has been described in detail with reference to preferred embodiments thereof. However, it will be appreciated that those skilled in the art, upon consideration of this disclosure, may make modifications and improvements within the spirit and scope of the invention.

What is claimed is:

1. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound that is an N,N'-disubstituted guanidine, N,N,N'-trisubstituted guanidine, N,N,N',N'-tetrasubstituted guanidine, or an N,N-disubstituted guanidine.

2. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formulae I:



I

wherein R and R' each are a substituted or unsubstituted alkyl group of at least 4 carbon atoms, substituted or unsubstituted carbocyclic aryl groups of at least 6 carbon atoms, or a substituted or unsubstituted heterocyclic aromatic ring.

3. The method of claim 2 wherein the compound of Formula I is N'-di-m-tolylguanidine; N,N'-di-o-iodophenylguanidine; N,N'-di-o-ethylphenylguanidine; N,N'-di-m-ethylphenylguanidine; N,N'-bis(2-iodophenyl)guanidine; N,N'-bis(3-tolyl)guanidine; N,N'-bis(3-ethylphenyl)guanidine; N,N'-bis(2-isopropylphenyl)guanidine; N,N'-bis(3-isopropylphenyl)guanidine; N,N'-bis(1-naphthyl)guanidine; N,N'-bis(3-methoxyphenyl)guanidine; N,N'-bis(3-trifluoromethylphenyl)guanidine; N,N'-bis(4-fluoro-3-ethylphenyl)guanidine; N,N'-bis(3,5-diethylphenyl)guanidine; N,N'-bis(3-nitrophenyl)guanidine; N,N'-bis(4-fluoro-3-nitrophenyl)guanidine; N,N'-bis(3-nitro-5-ethylphenyl)guanidine; N,N'-bis(3-azidophenyl)guanidine; N,N'-bis(quinolin-8-yl)guanidine; N,N'-bis(coumarin-8-yl)guanidine; N,N'-dibutylguanidine; N'N'-diphenylguanidine; N,N'-di-o-tolylguanidine; N,N'-di-(2-methyl-4-bromophenyl)guanidine; N,N'-di-(2-methyl-4-iodophenyl)guanidine; N,N'-di(cyclohexyl)guanidine; N,N'-di-(m-propylphenyl)guanidine; N,N'-di-(1-tetralinyl)guanidine; N,N'-di(±-endo-2-norbornyl)guanidine; N,N'-di-(exo-2-norbornyl)guanidine; N,N-di-(4-

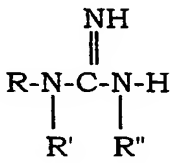
indanyl)guanidine; N,N'-diadamantylguanidine; N,N'-dibenzylguanidine; N-(1-naphthyl)-N'-(o-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(m-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-methoxyphenyl)guanidine; N-(1-naphthyl)-N'-(4-indanyl)guanidine; N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-(m-ethylphenyl)'N'-(m-tolyl)guanidine; N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-methylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-tolyl)guanidine; N-(o-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(o-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-ethylphenyl)-N'-(4-indanyl)guanidine; N-(o-ethylphenyl)-N'-(m-ethylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-tolyl)guanidine; N-(o-iodophenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenylguanidine; N-(o-iodophenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-iodophenyl)-N'-(4-indanyl)guanidine; N-(o-iodophenyl)-N'-(o-ethylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(o-isopropylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(o-isopropylphenyl)-N'-(o-ethylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(m-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-isopropylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-methoxyphenyl)-N'-(m-tolyl)guanidine; N-(m-methoxyphenyl)-N'-(m-tolyl)guanidine; N-(2-4-di-iodo-5-hydroxyphenyl)-N'-(2-tolyl)guanidine; N-(1-naphthyl)-N'-(2-iodophenyl)guanidine; N-(1-naphthyl)-N'-(3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(3-tolyl)guanidine; N-(1-naphthyl)-N-(4-bromo-3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-nitro-3-ethylphenyl)guanidine;

N-(1-naphthyl)-N'-[3-(1-hydroxy-ethyl)phenyl]guanidine; N-(4-fluoronaphthyl)-N'-(3-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(1-naphthyl)-N'-(4-bromo-3-tolyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-tolyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(4-indanyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(m-ethylphenyl)guanidine; N-(m-trifluoromethylphenyl)-N'-(o-iodophenyl)guanidine; N-(1-naphthyl)N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(2-isopropylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(2-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-2-isopropylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-2-isopropylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(6-methoxy-3-ethylphenyl)guanidine; N-(4-fluoronaphthyl)-N'-(6-methoxy-4-fluoro-3-ethyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(7-fluoronaphthyl)-N'-(4-fluoro-3-tolyl)guanidine; N-(4-fluoronaphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(7-fluoronaphthyl)-N'-(4-fluoro-3-trifluoromethylphenyl)guanidine; N-(coumarin-8-yl)-N-(3-ethylphenyl)guanidine; N-(coumarin-8-yl)-N'-(3-tolyl)guanidine; N-(quinolin-8-yl)-N'-(3-ethylphenyl)guanidine; N-(quinolin-8-yl)-N'-(3-tolyl)guanidine; N-(cyclohexyl)-N'-(4-bromo-2-methylphenyl)guanidine; N-(1-naphthyl)-N'-(o-iodophenyl)guanidine; N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(o-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-tolylphenyl)guanidine; N-(1-naphthyl)-N'-(o-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(m-isopropylphenyl)guanidine; N-(1-naphthyl)-N'-(m-methoxyphenyl)guanidine; N-(1-naphthyl)-N'-(4-indanylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(m-ethylphenyl)-N'-(m-

ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-tolylphenyl)guanidine; N-(m-ethylphenyl)-N'-(o-ethylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(m-ethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-ethylphenyl)-N'-(4-indanylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-tolyl)guanidine; N-(o-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-(o-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-ethylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-ethylphenyl)-N'-(4-indanyl)guanidine; N-(o-iodophenyl)-N'-(m-tolyl)guanidine; N-(o-iodophenyl)-N'-(o-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-iodophenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-iodophenyl)-N'-(4-indanyl)guanidine; N-(o-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(o-isopropylphenyl)-N'-(m-isopropylphenyl)guanidine; N-(o-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(o-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-isopropylphenyl)-N'-(m-tolyl)guanidine; N-(m-isopropylphenyl)-N'-(m-methoxyphenyl)guanidine; N-(m-isopropylphenyl)-N'-(4-indanyl)guanidine; N-(m-methoxyphenyl)-N'-(m-tolyl)guanidine; N-(m-methoxyphenyl)-N'-(4-indanyl)guanidine; N-(4-indanyl)-N'-(m-tolyl)guanidine; N-(2-methylazidophenyl)-N'-(2-methylphenyl)guanidine; N-adamantyl-N'-(2-methylphenyl)guanidine; N-(iodophenyl)-N'-(2-methylphenyl)guanidine; N-(2-methyl-4-nitrophenyl)-N'-(2-methylphenyl)guanidine; N-(2-iodophenyl)-N'-(adamantyl)guanidine; N-(2-methylphenyl)-N'-(cyclohexyl)guanidine; N-adamantyl-N'-phenylguanidine; N-(3,5-dimethyl-1-adamantyl)-N'-(o-tolyl)guanidine; N-(3,5-dimethyl-1-adamantyl)-N'-(o-iodophenyl)guanidine; N-(1-adamantyl)-N'-(o-nitrophenyl)guanidine; N-(exo-2-isobornyl)-N'-(o-iodophenyl)guanidine; N-(exo-2-isobornyl)-N'-(o-tolyl)guanidine; N-(o-iodophenyl)-N'-(t-butyl)guanidine; N-(adamant-1-yl)-N'-(o-isopropylphenyl)guanidine; N-(adamant-1-yl)-N'-(p-bromo-o-tolyl)guanidine; N-(cyclohexyl)-N'-(p-bromo-o-tolyl)guanidine; N-(adamant-2-yl)-N'-(p-iodophenyl)guanidine; N-(adamantan-1-yl)-N'-(2-trifluoromethylphenyl)guanidine; N-(adamantan-1-yl)-N'-(2-methylphenyl)-

N'-methylguanidine; N-(adamantan-1-yl)-N'-(6-coumarinyl)guanidine; N-(adamantan-1-yl)-N'-(8-coumarinyl)guanidine; N-(adamantan-1-yl)-N'-(2,4-difluorophenyl)guanidine; and N-(adamantan-1-yl)-N'-(2-trifluoromethyl-4-fluorophenyl)guanidine; and pharmaceutically acceptable salts of said compounds.

4. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formulae II:



II

wherein R, R' and R" are independently a C_1-C_8 alkyl group, a C_2-C_8 alkenyl group, C_2-C_8 alkynyl group, cycloalkyl group, cycloalkyl group substituted by one or more substituents, cycloalkenyl group, cycloalkenyl group substituted with one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted by one or more substituents, alkaryl group, alkaryl group substituted by one or more substituents, heterocyclic group, heterocyclic group substituted by one or more substituents, heteroaryl group, or a heteroaryl group substituted by one or more substituents;

or a physiologically acceptable salt thereof;

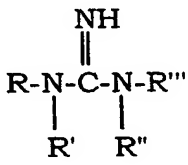
wherein said substituent is chloro, fluoro, bromo, iodo, C_1-C_8 alkyl, C_1-C_8 alkoxy, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_8 alkylthio, allyl, aralkyl, alkaryl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_8 acyl, aryl, heteroaryl, an aryl fused to a benzene ring, a heteroaryl fused to a benzene ring, C_3-C_6 heterocycloalkyl, a C_3-C_6 heterocycloalkyl ring fused to a benzene ring, C_1-C_8 alkylsulfonyl, arylthio, amino, C_1-C_8 alkylamino, C_2-C_{15} dialkylamino, hydroxy, hydroxyalkyl, carbamoyl, C_1-C_8 N-alkylcarbamoyl, C_2-C_{15} N,N'-dialkylcarbamoyl, nitro, azido or a C_2-C_{15} dialkylsulfamoyl.

5. The method of claim 4 wherein the compound of Formula II is N,N'-di-(1-naphthyl)-N-methylguanidine; N,N'-di-(1-naphthyl)-N-ethylguanidine; N,N'-di-(m-ethylphenyl)-N-methylguanidine; N-(o-isopropylphenyl)-N'-methyl-N'-(1-naphthyl)guanidine; N-(m-ethylphenyl)-N-methyl-N'-(1-naphthyl)guanidine; N-ethyl-N,N'-di-(m-ethylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-ethyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-ethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N,N'-di-(m-ethylphenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-(isopropyl)-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N-isopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-isopropyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-isopropyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N-methyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-methyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-

isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N-ethylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N'-methylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(2-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(5-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(8-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(6-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,4-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,6-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,4,6-trifluoro-3-ethylphenyl)-N'-methylguanidine; N-(2,4-difluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4-difluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4,5-trifluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(2,4,8-trifluoro-1-naphthyl)-N'-(3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(2,6-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(2,4-difluoro-3-ethylphenyl)-N'-methylguanidine; N-(7-fluoro-1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(4-fluoro-1-naphthyl)-N'-(6-fluoro-3-ethylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N'-ethylguanidine; N-(1-naphthyl)-N'-(8-coumarinyl)-N-ethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(4-fluoro-3-ethylphenyl)-N'-methylguanidine; N,N'-di(8-coumarinyl)-N-methylguanidine; N,N'-di(8-coumarinyl)-N-ethylguanidine; N-(2-fluoronaphthyl)-N'-(3-

methylphenyl)-N'-methylguanidine; N-(4-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(5-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(7-fluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4-difluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4,5-trifluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(2,4,8-trifluoronaphthyl)-N'-(3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(5-fluoro-3-methylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N'-ethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(8-coumarinyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N'-ethylguanidine; and N-(8-coumarinyl)-N'-(3-trifluoromethylphenyl)-N'-ethylguanidine.

6. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formulae III:



III

wherein R, R', R" and R"' are independently a C_1-C_8 alkyl group, a C_2-C_8 alkenyl group, C_2-C_6 alkynyl group, cycloalkyl group, cycloalkyl group substituted by one or more substituents, cycloalkenyl group, cycloalkenyl group substituted with one or more substituents, carbocyclic aryl group, carbocyclic aryl group substituted by one or more substituents, alkaryl group, alkaryl group substituted by one or more substituents, heterocyclic group, heterocyclic group substituted by one or more substituents, heteroaryl group, or a heteroaryl group substituted by one or more substituents;

or a physiologically acceptable salt thereof;

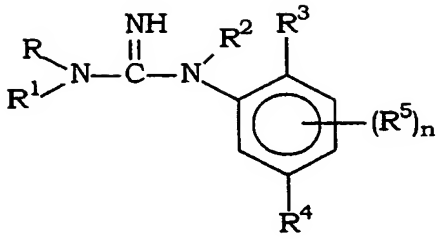
wherein said substituent is chloro, fluoro, bromo, iodo, C_1-C_8 alkyl, C_1-C_8 alkoxy, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_8 alkylthio, allyl, aralkyl, alkaryl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_8 acyl, aryl, heteroaryl, an aryl fused to a benzene ring, a heteroaryl fused to a benzene ring, C_3-C_6 heterocycloalkyl, a C_3-C_6 heterocycloalkyl ring fused to a benzene ring, C_1-C_8 alkylsulfonyl, arylthio, amino, C_1-C_8 alkylamino, C_2-C_{15} dialkylamino, hydroxy, hydroxyalkyl, carbamoyl, C_1-C_8 N-alkylcarbamoyl, C_2-C_{15} N,N'-dialkylcarbamoyl, nitro, azido or a C_2-C_{15} dialkylsulfamoyl.

7. The method of claim 6 wherein the compound of Formula III is N,N'-diethyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-diethyl-N,N'-di-(1-naphthyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N,N'-diethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N,N'-dimethyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-dimethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N-ethyl-N'-isopropyl-N,N'-di-(m-ethylphenyl)guanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-

isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-isopropylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-isopropylguanidine; N-ethyl-N-(4-indanyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(4-indenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(1-naphthyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-ethyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N,N'-diisopropyl-N,N'-di-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indanyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(4-indenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(1-naphthyl)guanidine; N,N'-diisopropyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)guanidine; N,N'-diisopropyl-N-(4-indanyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(4-indenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl)-N-(o-iodophenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(1-naphthyl)-N'-(m-ethylphenyl)guanidine; N,N'-diisopropyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)guanidine; N-methyl-N,N'-di-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-isopropylguanidine; N-methyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-isopropylguanidine; N-methyl-N-(4-indanyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(4-indenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(o-iodophenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(o-isopropylphenyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(1-naphthyl)-N'-(m-ethylphenyl)-N'-isopropylguanidine; N-methyl-N-(m-methylphenyl)-N'-(m-ethylphenyl)-N'-

isopropylguanidine; N-ethyl-N,N'-di-(m-ethylphenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indanyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(4-indenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-iodophenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(o-isopropylphenyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(1-naphthyl)-N'-methylguanidine; N-ethyl-N-(m-ethylphenyl)-N'-(m-methylphenyl)-N'-methylguanidine; N,N'-di(1-naphthyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-ethylphenyl)-N,N-dimethylguanidine; N,N'-di(8-coumarinyl)-N,N'-dimethylguanidine; N,N'-di(8-coumarinyl)-N-methyl-N'-ethylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N'-(3-azidophenyl)-N,N'-dimethylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-dimethylphenylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N,N'-dimethylguanidine; N-(8-coumarinyl)-N-(3-methylphenyl)-N,N'-dimethylguanidine; N-(1-naphthyl)-N'-(3-nitrophenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(3-azidophenyl)-N,N'-diethylguanidine; N-(8-coumarinyl)-N'-(3-nitrophenyl)-N,N'-diethylguanidine; N-(8-coumarinyl)-N'-(3-azidophenyl)-N,N'-diethylguanidine; N-(7-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-diethylphenylguanidine; N-(4-fluoro-1-naphthyl)-N'-(3-ethylphenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(4-fluoro-3-ethylphenyl)-N,N'-diethylguanidine; N-(1-naphthyl)-N'-(3-methylphenyl)-N,N'-diethylguanidine; and N-(8-coumarinyl)-N-(3-methylphenyl)-N,N'-diethylguanidine.

8. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formulae IV:



IV

wherein R, R^1 and R^2 are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted aminoalkyl, substituted or unsubstituted carbocyclic aryl, substituted or unsubstituted aralkyl, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R^3, R^4, and each R^5 substituent are each independently halogen, hydroxyl, azido, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted alkoxy, substituted or unsubstituted alkylthio, substituted or unsubstituted alkylsulfinyl, substituted or unsubstituted alkylsulfonyl, substituted or unsubstituted aminoalkyl, substituted or unsubstituted carbocyclic aryl, substituted or unsubstituted aralkyl, nitro, cyano, substituted or unsubstituted alkanoyl, or substituted or unsubstituted carboxy; n is an integer of from 0 to 3; or a pharmaceutically acceptable salt thereof.

9. The method of claim 8 wherein the compound of Formula IV is N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,5-dichlorophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N'-(2,5-dichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-

ethylphenyl)-N-methyl-N'-(2-chloro-5-trifluromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-trifluromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-fluoro-5-trifluromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-fluoro-5-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-methylphenyl); N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-methylthio)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-methylthio)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(1-naphthyl-N'-(2-fluoro-5-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2-fluoro-5-methylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,4,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,4,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2,3,5-trichlorophenyl)guanidine; N-(3-ethylphenyl)-N'-(2,3,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,4,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,3,5-trichlorophenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dichlorophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dimethylphenyl)guanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylphenyl)-N'-

methylguanidine; N-(1-naphthyl)-N'-(2-5-dimethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)-N-methylguanidine; N-(1-naphthyl)-N'-(2,5-dibromophenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(2-chloro-5-thiomethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-fluoro-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-thiomethyl-5-trifluoromethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-methoxy-5-methylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-ethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-methyl-N'-(2-chloro-5-thiomethylphenyl)guanidine; N-(8-quinolinyl)-N'-(2-chloro-5-methylphenyl)guanidine; N-(8-quinolinyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(8-quinolinyl)-N'-methyl-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl-N'-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-

trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2,5-dichlorophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N'-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-bromophenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-methyl-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-trifluoromethoxyphenyl)-N'-(2-bromo-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N-methyl-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-iodophenyl)-N'-methyl-N'-(2-chloro-5-

methylthiophenyl)guanidine; N-(3-iodophenyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(3-iodophenyl)-N-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N'-methyl-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-iodophenyl)-N'-(2-chloro-5-ethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-ethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-

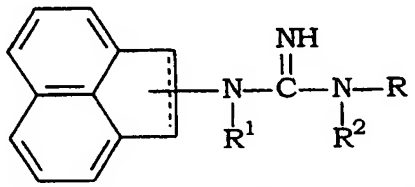
trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-chloro-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N'-methyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(3-trifluoromethylphenyl)-N,N'-dimethyl-N'-(2-bromo-5-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-chloro-5-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-iodo-5-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(2-bromo-5-methylthiophenyl)guanidine; N-(3-methylsulfonylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfonylphenyl)-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfinylphenyl)-N-methyl-N'-(2,5-dibromophenyl)guanidine; N-(3-methylsulfinylphenyl)-N'-(2,5-dibromophenyl)guanidine; or a pharmaceutically acceptable salt thereof.

10. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of claim 1, 4, 6 or 8 that has a substituent of carbocyclic aryl substituted at one or more ring positions by haloalkyl, substituted or unsubstituted thioalkyl having from 1 to about 3 carbon atoms, substituted or unsubstituted alkylsulfinyl or substituted or unsubstituted alkylsulfonyl.

11. The method of claim 10 wherein the compound is N-(1-naphthyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-methylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfinylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfinylphenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfonylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N'-(3-methylsulfonylphenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylthiophenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethylthiophenyl)guanidine; N-(1-naphthyl)-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N,N'-dimethyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N'-(3-pentafluoroethylphenyl)guanidine; N-(1-naphthyl)-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(1-naphthyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfinylphenyl)-

N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylsulfinylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfinylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfonylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-methylsulfonylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-methylsulfonylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylthiophenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylthiophenyl)guanidine; N-(3-ethylphenyl)-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-pentafluoroethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-pentafluoroethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-(3-pentafluoroethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)-N'-methylguanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethoxyphenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-methylthiophenyl)-N'-methylguanidine; N-(3-methylthiophenyl)-N-methyl-N'-(3-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(3-methylthiophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-bromophenyl)guanidine; N-(3-methylthiophenyl)-N'-(3-bromophenyl)-N'-methylguanidine; N-(3-methylthiophenyl)-N-methyl-N'-(3-bromophenyl)guanidine; N-(3-methylthiophenyl)-N,N'-dimethyl-N'-(3-bromophenyl)guanidine; N-(3-ethylphenyl)-N,N'-dimethyl(3-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N-methyl-N'-(3-trifluoromethylphenyl)guanidine; N-(3-ethylphenyl)-N'-(3-trifluoromethylphenyl)-N'-methylguanidine; N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N-methylguanidine; or N-(1-naphthyl)-N'-(3-trifluoromethylphenyl)-N,N'-dimethylguanidine; or a pharmaceutically acceptable salts thereof.

12. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula V:

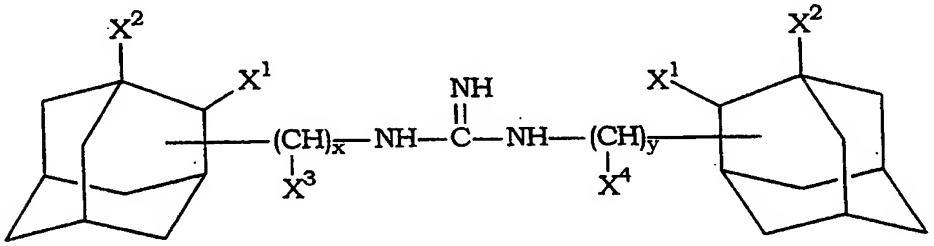


V

wherein R is cycloalkyl; carbocyclic aryl; alkaryl; aralkyl or heterocyclic; R^1 and R^2 are the same or different and selected from the group consisting of hydrogen, lower C_{1-6} alkyl, lower C_{1-6} alkylamino, C_{5-10} aryl or substituted aryl;

wherein R and the acenaphthyl group are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido; and pharmaceutically acceptable salts thereof.

13. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula VI:

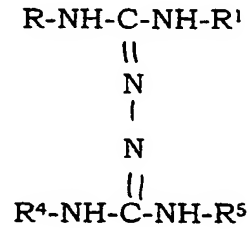


VI

wherein X^1, X^2, X^3, and X^4 are the same or different and are selected from the group consisting of hydrogen, hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro,

azido, sulfhydryl, cyano, isocynato, halogen, amido, sulfonato or carbamido; wherein at least one of X^1, X^2, X^3, and X^4 is other than hydrogen; x and y are the same or different and are 0, 1, 2, 3 or 4; and pharmaceutically acceptable salts thereof.

14. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula VII:



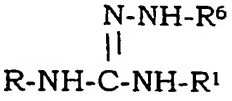
VII

or a tautomer thereof,

wherein R, R^1, R^4 and R^5 are the same or different and are cycloalkyl; carbocyclic aryl, alkaryl; aralkyl; or heterocyclic;

wherein R, R^1, R^4 or R^5 is optionally substituted hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido; or pharmaceutically acceptable salt thereof.

15. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formula:



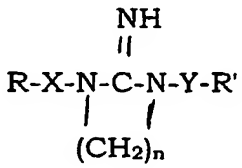
or a tautomer thereof,

wherein R and R^1 are the same or different and are cycloalkyl; carbocyclic aryl; alkaryl; aralkyl; heterocyclic;

wherein R and R^1 are optionally substituted by hydroxy, acetate, oxo, amino, lower C_{1-6} alkyl, lower C_{1-6} alkyl amino, alkoxy of 1-6 carbon atoms, di-lower C_{2-12} alkyl amino, nitro, azido, sulfhydryl, cyano, isocyanato, halogen, amido, sulfonato or carbamido;

R^6 is hydrogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, carbocyclic aryl, nitrile, C_1-C_6 alkoxycarbonyl, C_1-C_6 acyl or benzoyl; or pharmaceutically acceptable salts thereof.

16. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula XI:



XI

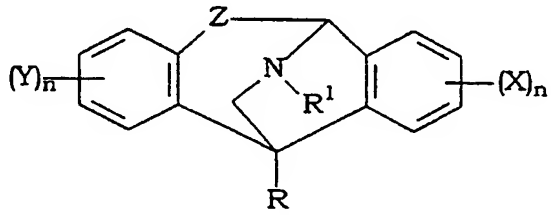
wherein

n is 2, 3, 4 or 5;

X and Y are independently a single bond, a branched or straight chain C_1-C_{12} alkylene or a branched or straight chain alkenylene;

R and R' are independently hydrogen, substituted or unsubstituted a cycloalkyl group of at least 3 carbons, a substituted or unsubstituted carbocyclic group of at least 6 carbon atoms, particularly substituted or unsubstituted phenyl; substituted or unsubstituted aralkyl of at least 6 carbon atoms and containing 1-3 separate or fused rings, or a substituted or unsubstituted heterocyclic or heteroaromatic group having from 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms, and wherein each of R and R' may be substituted; or wherein R and R' together with the guanidine nitrogen to which they are attached form a saturated or unsaturated cyclic ring containing at least 2 carbon atoms exclusive of the guanidine carbon atom, and wherein said cyclic ring may be substituted with one or more alkyl groups of 1-6 carbon atoms, carbocyclic aryl or at least 6 carbon atoms, cycloalkyl groups of 3-12 carbon atoms, or 1-2 fused aromatic rings; and pharmaceutically acceptable salts thereof.

17. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula XII:



XII

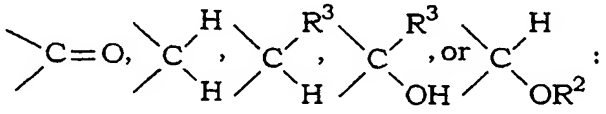
wherein:

R is hydrogen, C_2-C_6 acyl, C_1-C_6 alkyl, aryl, C_1-C_6 alkoxycarbonyl, C_7-C_{10} aralkyl, C_2-C_6 alkenyl, C_3-C_{15} dialkylaminoalkyl, C_1-C_6 hydroxyalkyl, C_2-C_6 alkynyl, C_3-C_{15} trialkylsilyl, C_4-/C_{10} alkylcycloalkyl, or C_3-C_6 cycloalkyl;

R^1 hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_7-C_{10} aralkyl, C_1-C_6 alkoxy, C_1-C_6 alkylamino, or C_3-C_{15} dialkylaminoalkyl;

X and Y are independently selected from the group consisting of a halogen such as chloro, fluoro, bromo, iodo, C_1-C_6 alkoxy, C_2-C_6 dialkoxymethyl, C_1-C_6 alkyl, cyano, C_3-C_{15} dialkylaminoalkyl, carboxy, carboxamido, C_1-C_6 haloalkyl, e.g. trifluoromethyl; C_1-C_6 haloalkylthio, allyl, aralkyl, C_3-C_6 cycloalkyl, aroyl, aralkoxy, C_2-C_6 acyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, C_3-C_6 heterocycloalkyl, C_1-C_6 alkylthio, C_1-C_6 alkylsulfonyl, C_1-C_6 haloalkylsulfonyl, C_1-C_6 alkylsulfinyl, C_1-C_6 haloalkylsulfinyl, arylthio, C_1-C_6 haloalkoxy, amino, C_1-C_6 alkylamino, C_2-C_{15} dialkylamino, hydroxy, carbamoyl, C_1-C_6 N-alkylcarbamoyl, C_2-C_{15} N,N-dialkylcarbamoyl, nitro and C_2-C_{15} dialkylsulfamoyl;

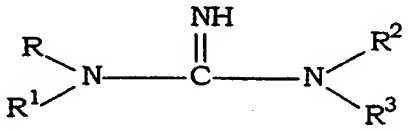
Z represents a group selected from



wherein R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, aralkyl, C_4-C_{15} dialkylaminoalkyl, heterocycloalkyl, C_2-C_6 acyl, aroyl, or aralkanoyl, and R^3 is C_1-C_6 alkyl, C_2-C_6 alkenyl, phenyl, aralkyl or C_3-C_{15} dialkylaminoalkyl; and

n is an integer selected from 0 (X or Y is hydrogen, respectively), 1, 2, 3 or 4, or a pharmaceutically acceptable salt thereof.

18. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of Formula XIII:



XIII

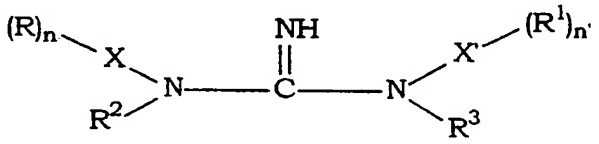
wherein:

R and R^1 are each independently substituted or unsubstituted alkyl; substituted or unsubstituted alkenyl; substituted or unsubstituted alkynyl; substituted or unsubstituted alkoxy; substituted or unsubstituted aminoalkyl; substituted or unsubstituted alkylthio; substituted or unsubstituted alkylsulfinyl; substituted or unsubstituted carbocyclic aryl; substituted or unsubstituted aralkyl; or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having from 1 to 3 rings, 3 to 8 ring members in each ring and from 1 to 3 heteroatoms, with at least one of R and R^1 being carbocyclic aryl, aralkyl, a heteroaromatic group or a heterocyclic group;

R^2 and R^3 each being independently selected from the group consisting of hydrogen, substituted and unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted and unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted and unsubstituted alkylsulfonyl having from 1 to about 20 carbon atoms, and

substituted and unsubstituted aminoalkyl; and pharmaceutically acceptable salts thereof.

19. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of the following Formula XIV:



XIV

wherein R and R^1 are each independently substituted or unsubstituted alkyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkenyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkynyl having from 2 to about 20 carbon atoms, substituted or unsubstituted alkoxy having from 1 to about 20 carbon atoms, substituted or unsubstituted aryloxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aralkoxy having from 6 to about 20 carbon atoms, substituted or unsubstituted aminoalkyl having 1 to about 20 carbon atoms, substituted or unsubstituted alkylthio having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfinyl having from 1 to about 20 carbon atoms, substituted or unsubstituted alkylsulfonyl having 1 to about 20 carbon atoms, substituted or unsubstituted carbocyclic aryl having at least 5 ring atoms, substituted or unsubstituted aralkyl having at least 5 ring atoms, or a substituted or unsubstituted heteroaromatic or heteroalicyclic group having 1 to 3 rings, 3 to 8 ring members in each ring and 1 to 3 heteroatoms;

R^2 and R^3 are each independently hydrogen or a group as defined for R and R^1 above, and preferably are each substituted or unsubstituted alkyl, alkenyl, alkynyl, alkoxy, aminoalkyl, alkylthio or alkylsulfinyl; or R^1 and R^3 together form a ring having 5 or more ring members;

n and n' independently are each equal to 1, 2, or 3;

X and X' are each independently a chemical bond (i.e., a bond between the guanidine nitrogen and R or R^1), substituted or unsubstituted alkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted alkenylene having from 2 to about 8 carbon atoms, or substituted or unsubstituted alkynylene having from 2 to about 8 carbon atoms, substituted or unsubstituted heteroalkylene having from 1 to about 8 carbon atoms, substituted or unsubstituted heteroalkenylene having 2 to about 8 carbon atoms, and substituted or unsubstituted heteroalkynylene having from 2 to about 8 carbon atoms, with at least one X and X' being other than a bond; and pharmaceutically acceptable salts thereof.

20. A method for treating an infection in a mammal, comprising administering to a mammal suffering from or susceptible to an infection an effective amount of an aminoglycoside antibiotic and a compound of any one of Formulae XV through XV as defined above.

21. The method of any one of claims 1-20 wherein the mammal is suffering from an infection of a Gram negative bacteria.

22. The method of any one of claims 1-20 wherein the mammal is suffering from an infection of a Gram positive bacteria.

23. The method of any one of claims 1-22 wherein the aminoglycoside antibiotic is gentamycin, amikacin, kanamycin, streptomycin, paromoycin, neomycin, netilmicin or tobramycin.

24. The method of any one of claims 1-22 wherein the aminoglycoside antibiotic is a seldomycin, sisomycin, aurimycin, lividomycin, streptothricin, hybrimycin, coralinomycin, butirosin, strepomutin, nebramycin, tenebrimycin, ribostamycin, destomycin, trehalosamine, myomycin, fortimicin, mutamicin or kasugamycin.

25. The method of any one of claims 1-24 wherein the compounds are administered substantially simultaneously to the mammal.

26. The method of any one of claims 1-24 wherein the compounds are administered as a unitary pharmaceutical formulation.

27. A pharmaceutical composition comprising a pharmaceutically acceptable carrier, an aminoglycoside antibiotic and a compound of formulae I through XXV as defined above.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/13640

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61K 31/13, 31/55; C07D 211/56, 211/98, 217/22

US CL :514/611, 634; 546/143, 244; 549/269; 564/108

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/611, 634; 546/143, 244; 549/269; 564/108

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5,221,693 A (SHETTY) 22 June, 1993. See the entire document especially Column 5, lines 40-43 and column 7, lines 15-19.	1-13, 18-19 and 21-27
Y	US 5,403,861 A (GOLDIN et al.) 04 April, 1995. See the entire document especially column 12, formula I.	1-13, 18-19 and 21-27

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"B"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 17 AUGUST 1998	Date of mailing of the international search report 29 SEP 1998
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer TAOFIQ A. SOLOLA Telephone No. (703) 308-1235

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/13640

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 20
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

The claim refer to formula XV which lacks proper antecedent basis.

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-13, 18-19 and 21-27

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/13640

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING
This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s)1-13, 18-19 and 21-27, drawn to compounds.
Group II, claim(s) 14-15, drawn to compounds.
Group III, claim 16, drawn to compounds.
Group IV, claim 16, drawn to compounds.
Group V, claim 16, drawn to compounds.
Group VI, claim 16, drawn to compounds.
Group VII, claim 17, drawn to compounds.

On page 120, two claims are numbered 14. The Examiner has renumbered the second claim 14 as claim 15 and subsequent claims are renumbered accordingly. There are now 27 claims. Above groupings reflect the new numbers.

The inventions of groups I-VII do not relate to a singe inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: all the compounds, except compounds of group VII, share guanidine which is known in the art.

The special technical feature in group I is that the guanidine has several substituents, such as quinoline, bromophenyl, iodophenyl, norbornyl, coumarin, etc. The special technical feature in group II is that the guanidine is substituted by an amine group, forming nitroguanidine central core or substituted by another guanidine, forming biguanidine central core. The special technical feature of group III is that the -N-C-N- group in the guanidine condensed with $-CH_2-CH_2-$ to form 2-nitroimidazoline as the central core. The special technical feature of group IV is that the -N-C-N- group in the guanidine condensed with $-CH_2-CH_2-CH_2-$ to form 2-nitropyrimidine as the central core. The special technical feature of group V is that the -N-C-N- group in the guanidine condensed with $-CH_2-CH_2-CH_2-CH_2-$ to form 2-nitro-1,3-diazopine as the central core. The special technical feature of group VI is that the -N-C-N- group in the guanidine condensed with $-CH_2-CH_2-CH_2-CH_2-CH_2-$ to form 2-nitro-1,3-diazocyclooctane as the central core. The special technical feature in group VII is that the central core contains benzoazopine having nitrogen bridge. The benzoazopine is further condensed with one benzene ring on each side to form a tetracyclic central core.